Methods of Computational Neuroscience

Part 3 of 6

Marine Biological Laboratory - Woods Hole, MA
August 2009

Day 4 (Aug. 6)

Ehud Ahissar

- Ahissar_MCN2009_partA.pdf
- Ahissar_MCN2009_partB.pdf
- Knutsen & Ahissar TINS 2009 + Erratum.pdf
- Diamond et al NRN 2008.pdf

David Kleinfeld (website)

- MCN_2009_1.pdf
- MCN_2009_2_online.pdf
- john_curtis_NN_touch_S1 .pdf
- david_Encyclopedia_of_Neuroscience.pdf
- david_ehud_mat_Current_Opinions_06.pdf

Day 5 (Aug 7)

Bill Spain

- MCN 09short.ppt
- Reading list for Bill Spain's seminar.doc
- Jeffress.pdf (one of the papers on the reading list that is not available online)

Week 2 (Aug. 10-14)

Day 1 (Aug 10)

Bard Ermentrout

- chapt1.pdf
- A very comprehensive tutorial on bifurcations for neuro
- A dated tutrial for XPP
- A very quick look at using xpp to solve the HH eqns
- A link to the xpp homepage

ml.ode Morris-Lecar ODE

hhh.ode Hodgkin-Huxley

Installation of XPP on your computer:

- Using XPP on windows

Adrienne Fairhall

- mcn2009Fairhall_2.pdf
- hongAgueraFairhallNC07.pdf
- lundstromFamulareFairhall.pdf
- agueraFairhallBialek.pdf
- hongLundstromFairhallPloSCB08.pdf
- lundstromNC08.pdf

Day 2 (Aug 11)

Dan Johnston

Day 3

Michael Hausser

- Hausser_slides.pdf
- Sjostrom_Hausser_Neuron06.pdf
- Hausser&London2005review.pdf

- mageeNatRevNeuro00.pdf

Bartlett Mel

- Mel_MCN_lecture.pdf

Day 4 (August 13)

Emre Aksay

- MCNTalk_2009_Aksay_Wiki.pptx

Mark Goldman

- Goldman_MCNTalk_Theory09.pdf

Day 5 (August 14)

Nancy Kopell

43:01

53:09

Sara A. Solla

123:21

- MBL09_SOLLA.ppt
- PRL04.pdf
- Chaos07.pdf

Week 3 (Aug. 17-21)

Day 1 (Aug. 17)

Karel Svoboda

- Svoboda_MCN.pdf

Larry Abbott

- AbbottLect1.pdf
- force5.pdf
- Bi, G.-q. & Poo, M.M. Synaptic modification by correlated activity: Hebb's postulate revisited. Annu. Rev. Neurosci. 24,139-166.
- Caporale N. & Dan, Y. Spike Timing-Dependent Plasticity: A Hebbian LearningRule. Annu. Rev. Neurosci. 31, 25-46 (2008).
- Dan Y. & Poo M.M. Spike timing-dependent plasticity: from synapse to perception. Physiol Rev. 86, 1033-1048 (2006).

Day 2 (August 18)

Sara Solla

Haim Sompolinsky:

- Learning spike based rules-THE TEMPOTRON
- guetig_sompolinsky06_full.pdf
- gutig_sompolinsky_plos09.pdf

Larry Abbott's second talk: Chaotic networks

- AbbottTalk2.pdf
  - Jaeger H., and Haas H. (2004). Harnessing nonlinearity: predicting chaotic systems and saving energy in wireless communication. Science 304, 78-80.

Day 3 (August 19)

Bence Olveczky

- woods hole09.pdf

Ila Fiete

- 2009_aug_MBL_birdsong_topost.pdf

Day 4 (August 20)

Reza Shadmehr

- Woods_hole_09_2.ppt

Emo Todorov

- MBL09.pdf

Day 5 (August 21)

Simon Laughlin

- mcn 09 simon.pdf

Week 4 (Aug. 24-28)

Day 1 (Aug. 24)

Mitya Chklovskii

- Theoretical Connectomics.pdf

Problem Sets

Week 1

Simulated Neurons

Problem Set 1.zip

See the papers from day 1 (Fairhall et al., 2006 and Pillow et al., 2008)

Information theory

ProblemSet-InformationTheory.pdf

ProblemSet-FisherInfoCorrelatedNeurons-MCN2009.pdf (updated 2009.08.11)

Solutions

ProblemSetSolution-InformationTheory-MCN2009.pdf (updated 2009.08.11)

ProblemSetSolution-FisherInfoCorrelatedNeurons-MCN2009.pdf

(updated 2009.08.11)

Spectral analysis

Link to Chronux download website

Kleinfeld_Mitra_CSHL_2009_revised..pdf

matlab_for mcn_2990.m

example_data.mat

whisking.mat

090606_PA5_noStim.mat

Week 2

Working with XPP

NOTE: These problems are to be done at your discretion, and will not be presented.

- tcurrent.ode Exploring T-current and bifurcations
- ping.ode A simple model for PING

These are text files. The instructions are at each individual file after the 'Done' statement.

NEURON tutorial and exercises

- NEURON Tutorial ppt.pdf
- NEURON short exercises.pdf
  - Complete these exercises to become familiar with NEURON, as well as gaining a better understanding of dendritic dynamics.
- simple_layerVpyramidal.zip

- Webpage for downloading NEURON to your computer
  - Follow the instructions for your OS of choice. At the computer stations in the lab we use the MacOS-X 10.4 version
  - For Mac laptops, you HAVE to install the XCode package (size is about 1GB). Please ask the TA's for it, before the tutorial on Wednesday.

NEURON mini projects

- NEURON mini projects.pdf
- Rall_MCN_Assignment.pdf
- Katz et al 2009 - Neuron.pdf
- Kampa & Stuart 2006 - JNeurosci.pdf

This version of the code contains an additional .hoc file for use with the second mini project. Open "exerciseS2.hoc" to access it.

mbl0813.zip

for problem 3:
Calcium spikes in basal dendrites (Kampa and Stuart 2006) [modelDB]

Attractor network exercises

Mark Goldman will discuss your solutions with you on Monday afternoon.

MCN_RecurrentNetsExercise.pdf

MCN 2009 Lecture Notes & Papers
Reader – Part 1 of 6

Week 1 (Aug. 3-7)

Day 1 (Aug. 3) - Reader – Part 1 of 6

Adrienne Fairhall

- mcn09FairhallSlides.pdf
- Fairhall2006.pdf (Covariance analysis in retina)
- Pillow2008.pdf (GLM analysis in retina)
- Fairhall-etal-01.pdf (Multiple timescale adaptation in the fly)
- lundstromNN08.pdf (Fractional differentiation in cortical neurons)
- MaravallPLOS07.pdf (Gain control in barrel cortex)
- ruderman1997.pdf (Review of natural scene statistics)

Bill Bialek (website)

- bialek_02.pdf Les Houches: *Thinking about the brain*
- The ideas about optimal motion estimation go back to a paper with Marc Potters, which can be found here: http://www.princeton.edu/~wbialek/our_papers/potters+bialek_94.pdf
- The material on photon counting in vision is covered in a set of lecture notes which can be found at

  http://www.princeton.edu/~wbialek/PHY562.html

Day 2 (Aug. 4) - Reader – Part 2 of 6

Jonathan Pillow

- pillow_slides09_MaxLi_GLM.pdf (lecture slides)

Michael Berry (website)

- MCN 2009 Populations.ppt
- Recording All Cells.pdf
- Redundancy in Retinal Code.pdf

Rava da Silveira

- TheOrchestralBrain-WithAnnotations.pdf

Day 3 (Aug. 5)

Roozbeh Kiani

- Kiani_CategorizationInIT.pdf
- kianiJNP07.pdf
- kianiNeuron08.pdf

Jim DiCarlo

- DiCarloWHslides.pdf

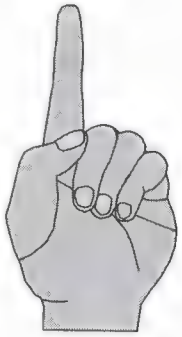
Elad Schneidman

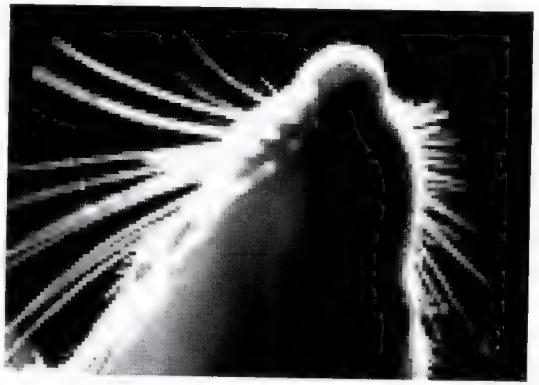
- Schneidman-MBL-MCN-2009.pdf
- Schneidman_2006_Nature_Weak pairwise correlations imply strongly.pdf
- Schneidman_PRL_2003_Network information and connected correlations.pdf
- Tkacik+al_06.pdf

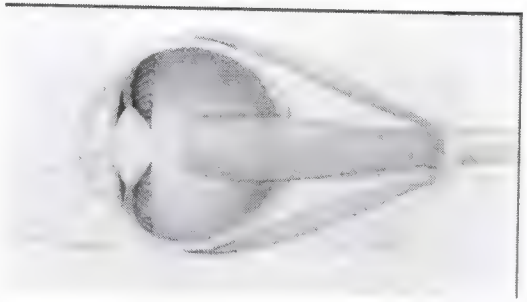
Closed loop control in active sensing

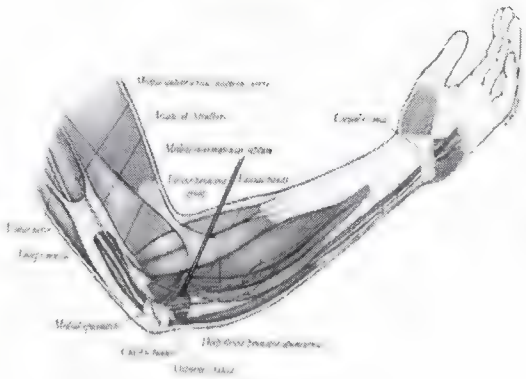
Active Sensing:

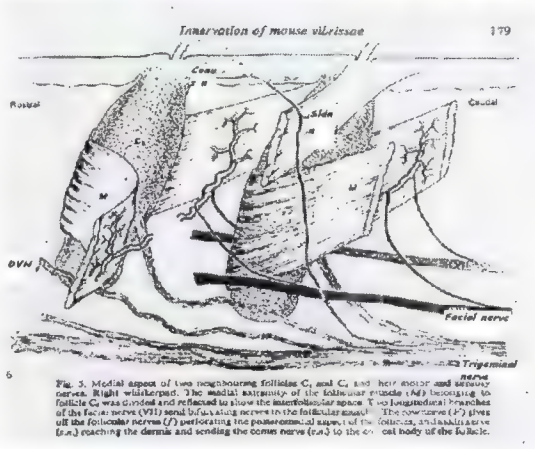
Sensor organs MOVE in order to obtain information











Why should sensory organ move?

- Receptors sense mostly changes
- Sensory sheets are not uniform

Object localization with whiskers

free_explor_250fr-sec uncompressed

Object localization with whiskers

free_explor_25fr-sec uncompressed

Object localization with whiskers

137_271003_1_37_B_50fps (task all whiskers) uncompressed

Object localization with whiskers

137_271003_1_37_B_50fps (task all whiskers) uncompressed

Object localization with whiskers

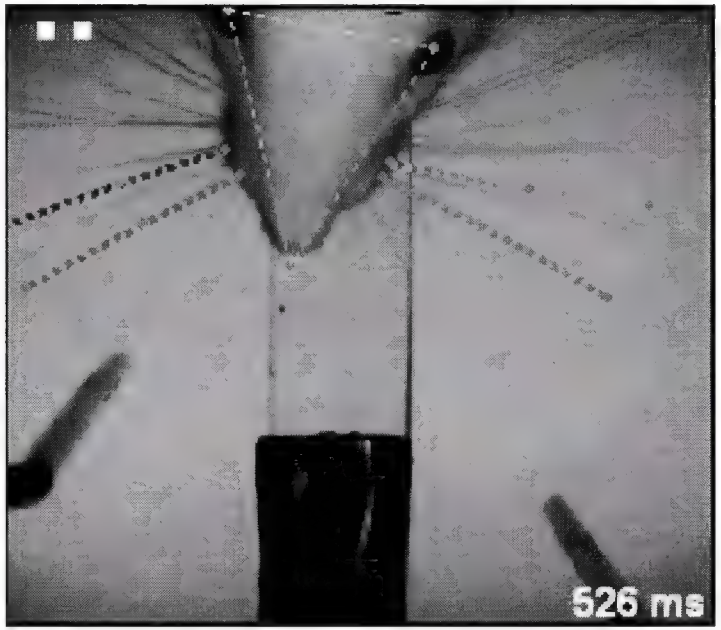
mode

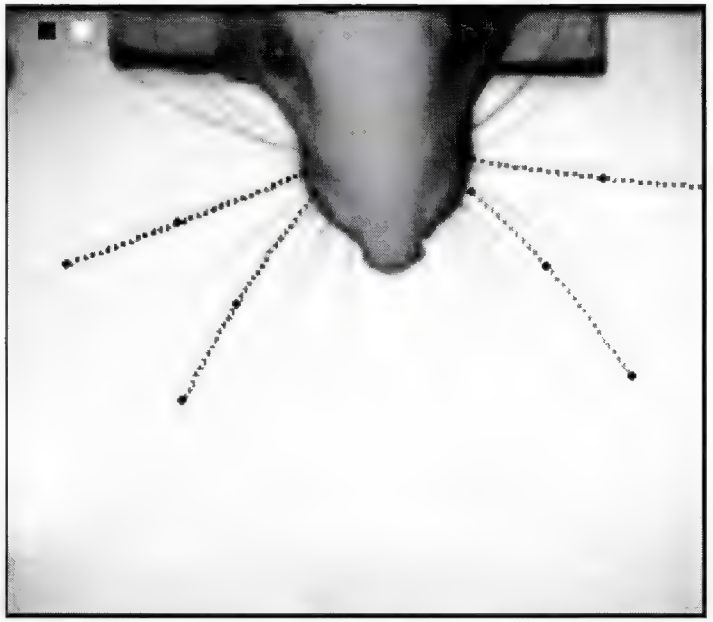
Per Knutsen and colleagues

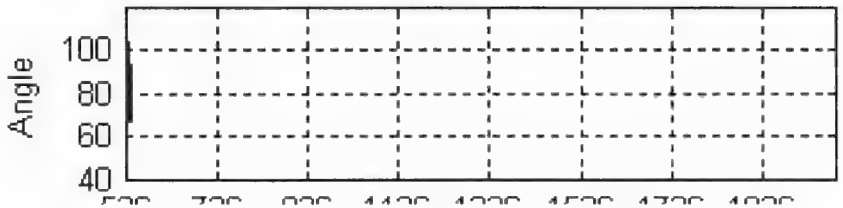
Ben Mitchinson, Tony Prescott, and colleagues

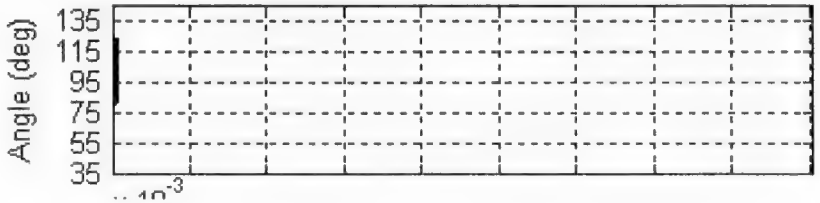
Object localization with whiskers

Context & contact





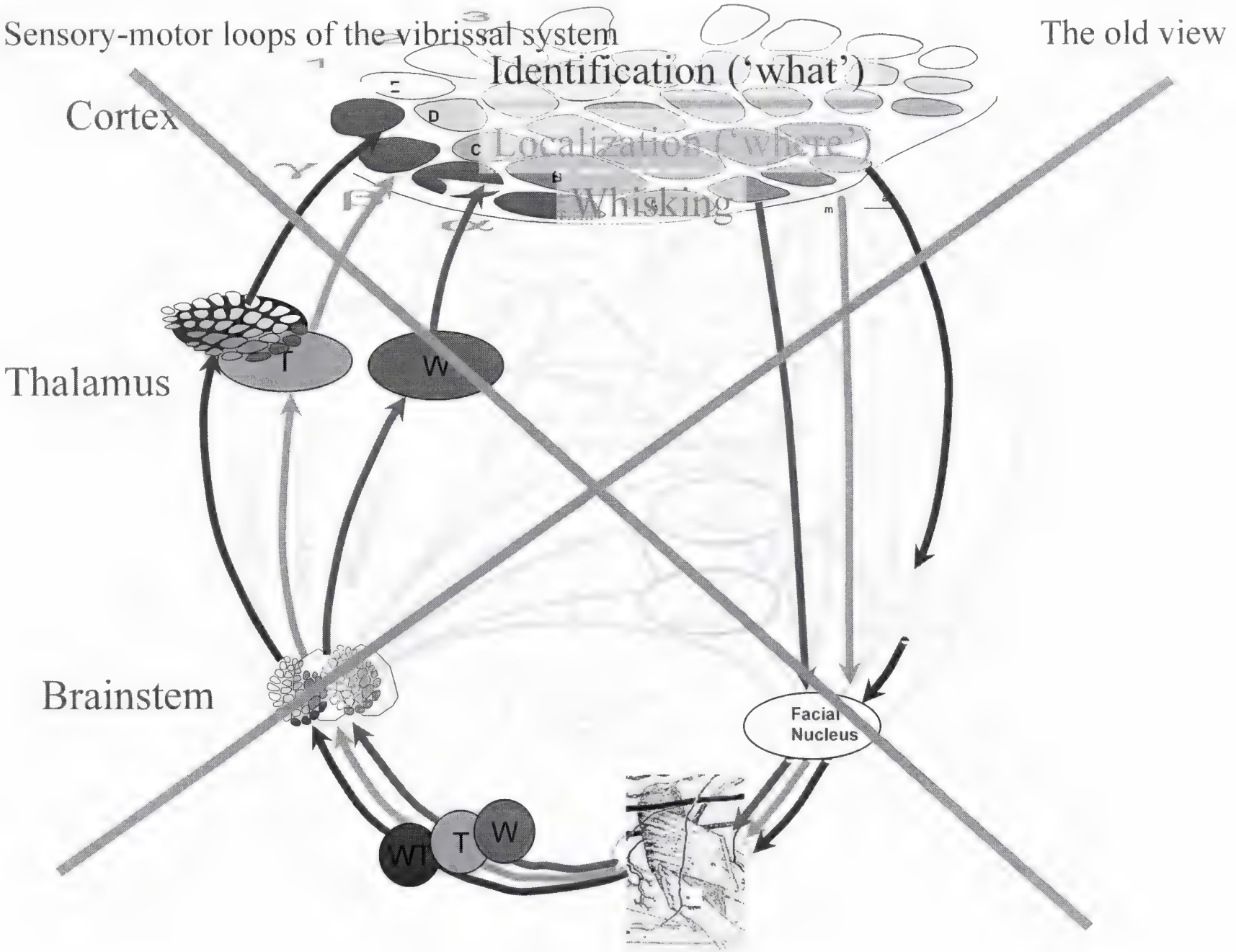


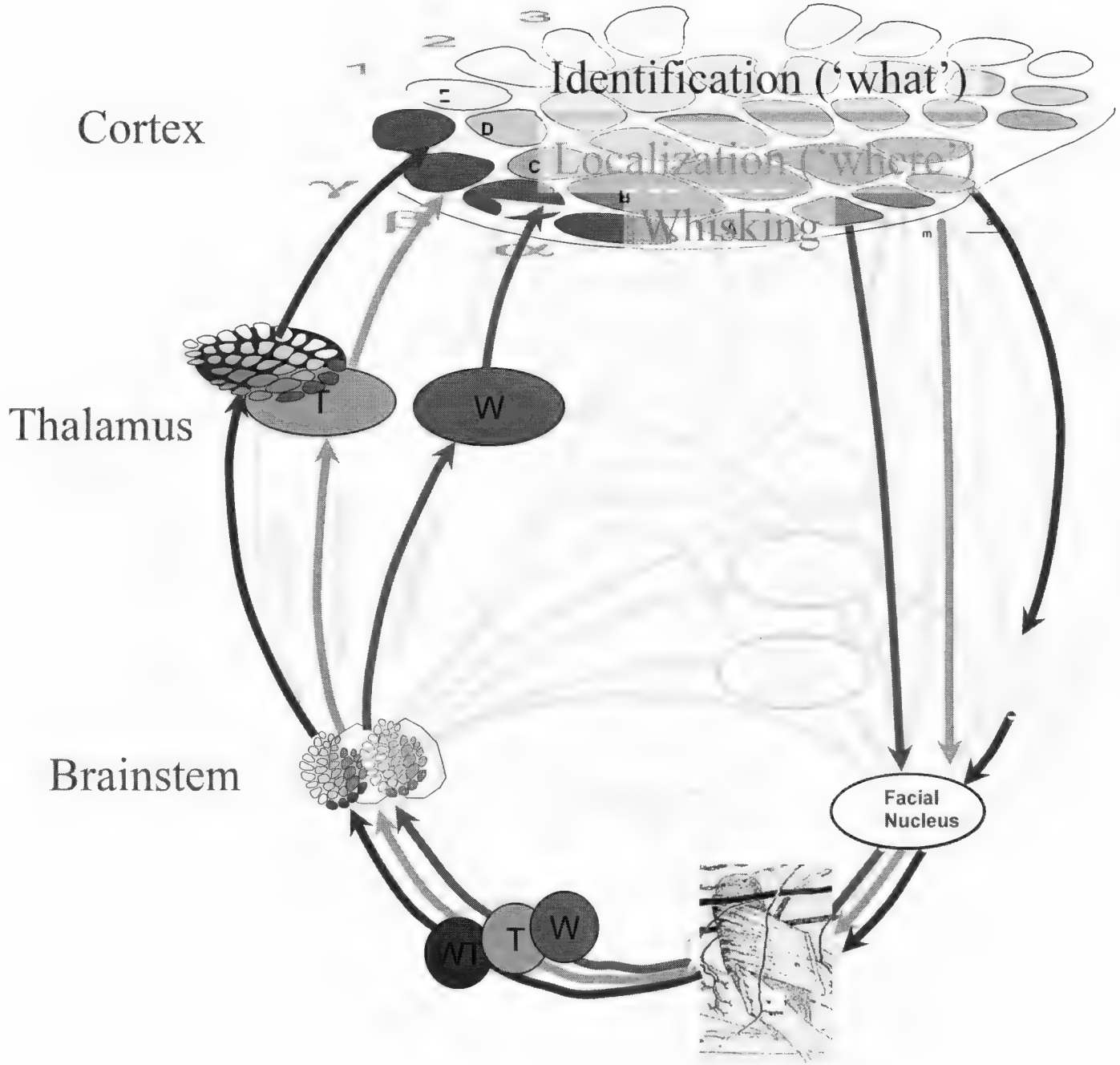


Object localization with whiskers

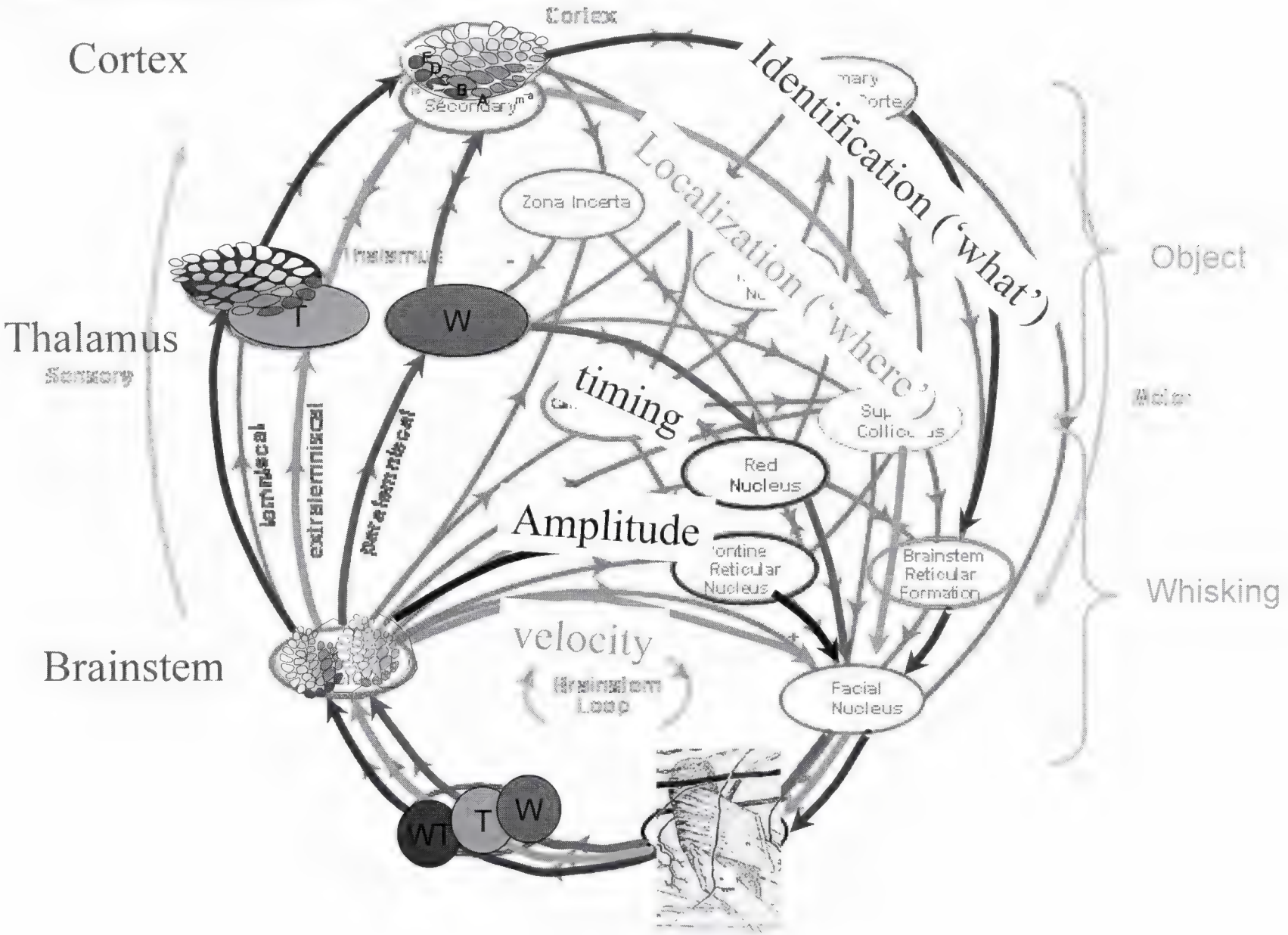
trial

Brain


Sensory-motor loops of the vibrissal system
The old view
Identification ('what')
Cortex
Localization ('where')
Whisking
Thalamus
T
W
Brainstem
Facial Nucleus
WT
T
W

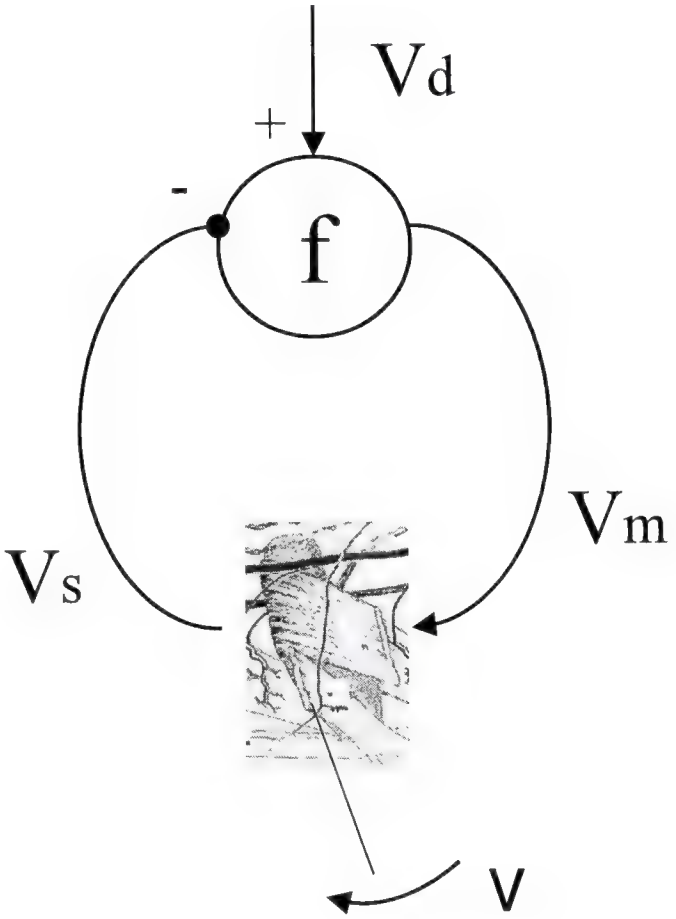

Identification ('what')
Cortex
Localization ('where')
Whisking
Thalamus
T
W
Brainstem
Facial
Nucleus
WT
T
W

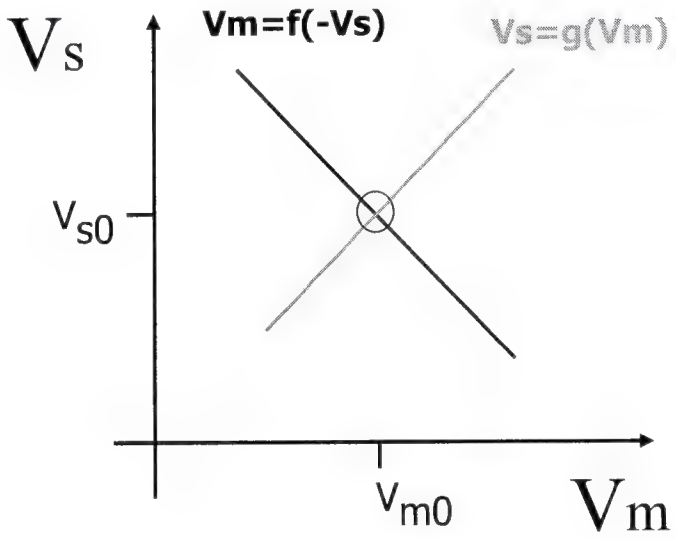
Sensory-motor loops of the vibrissal system



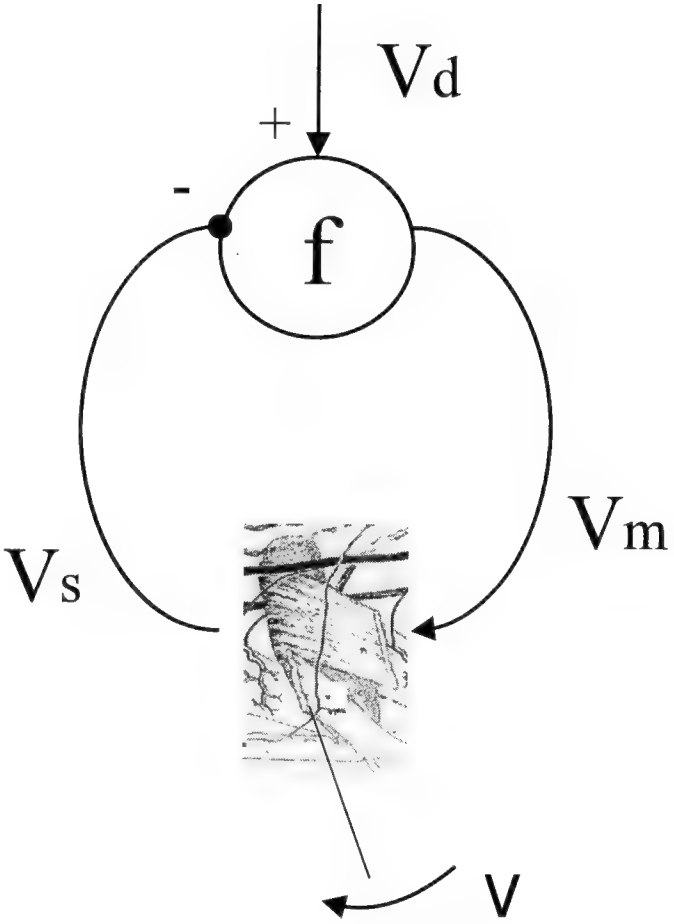
Basic principles of closed loop control

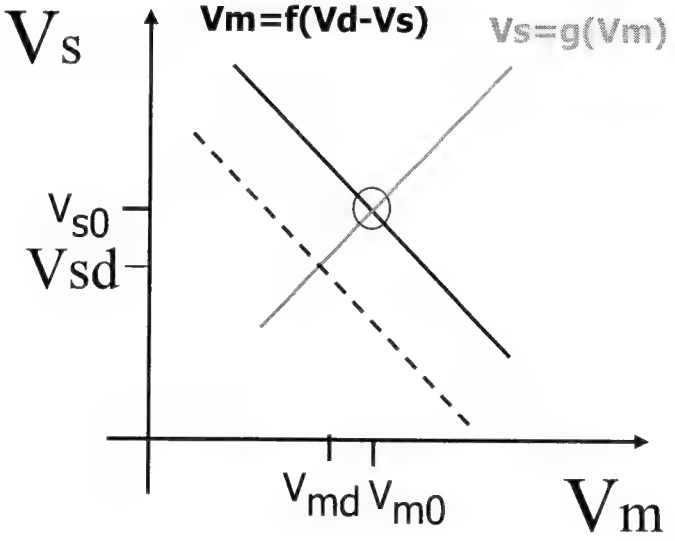
Set point



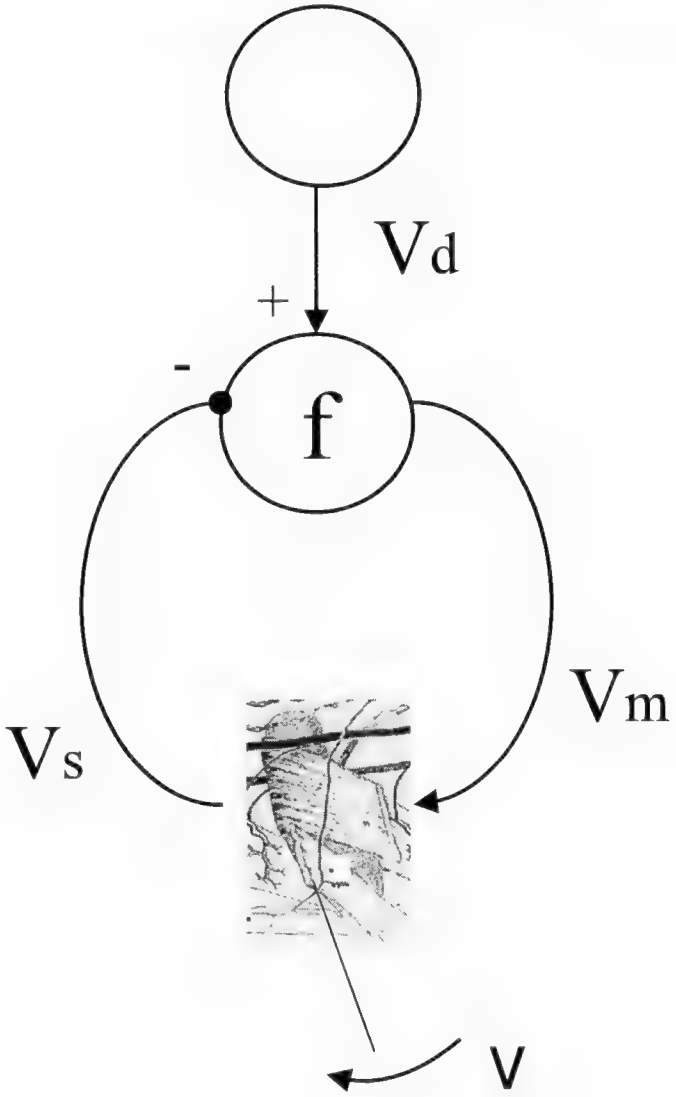


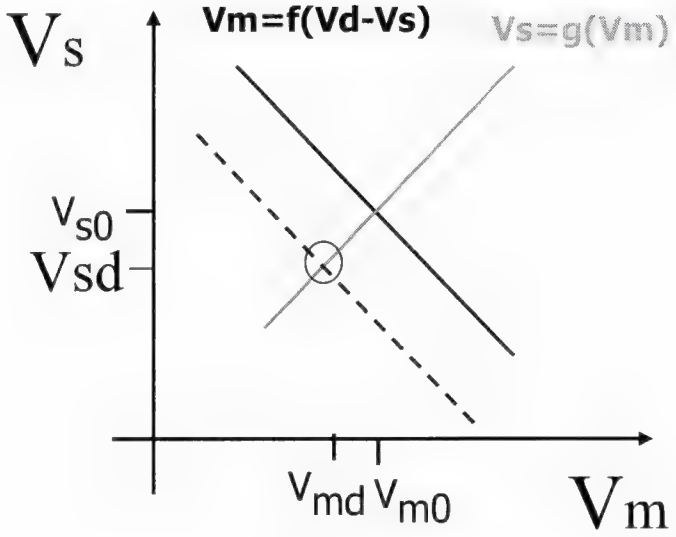
Set point



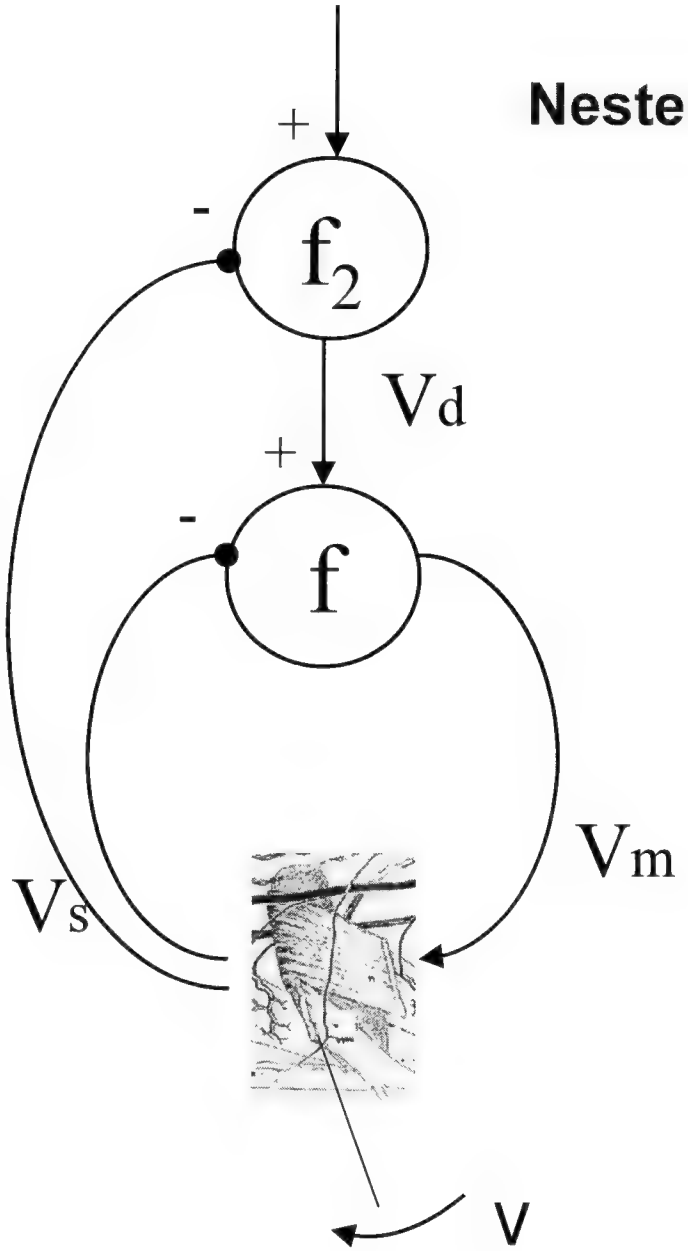


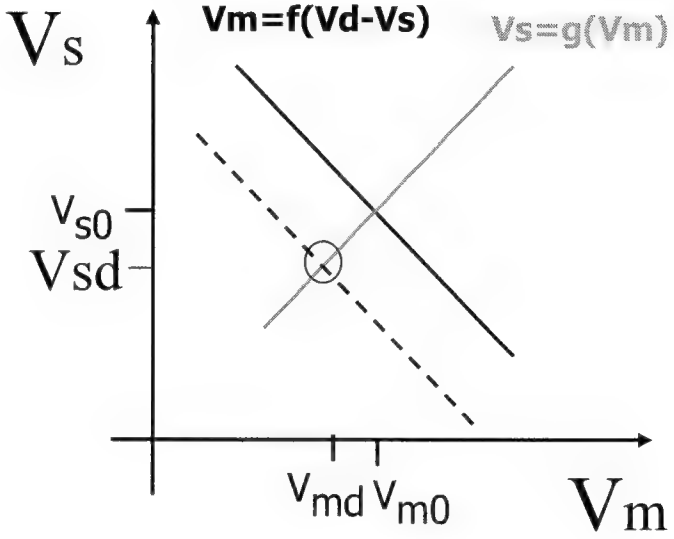
Direct control without direct connection



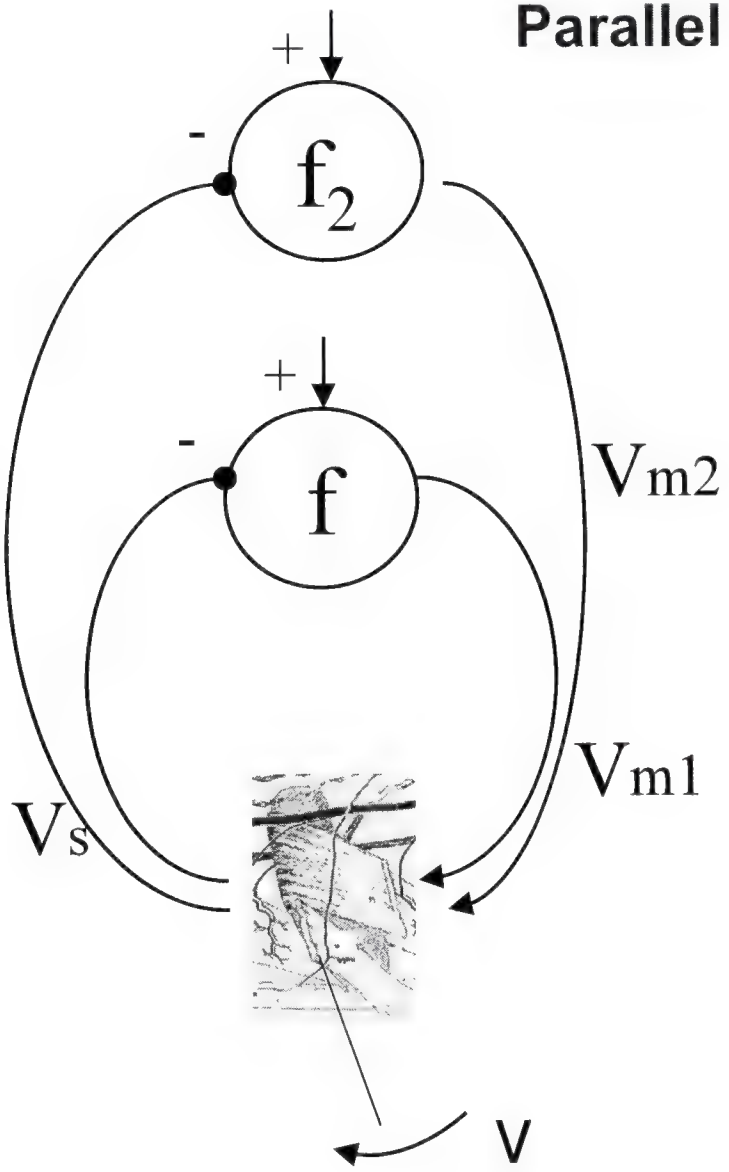


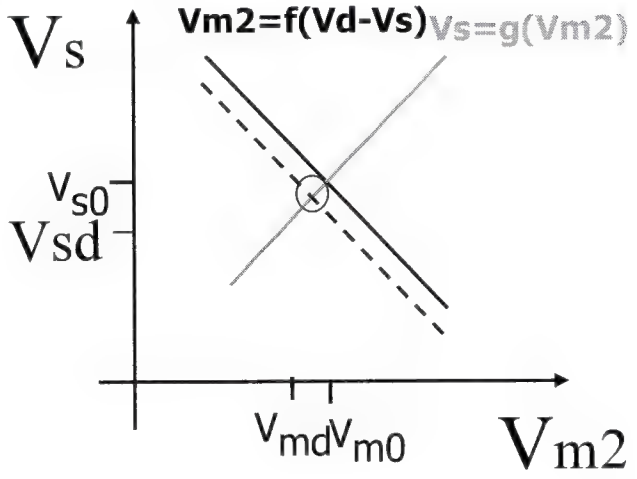
Nested loops

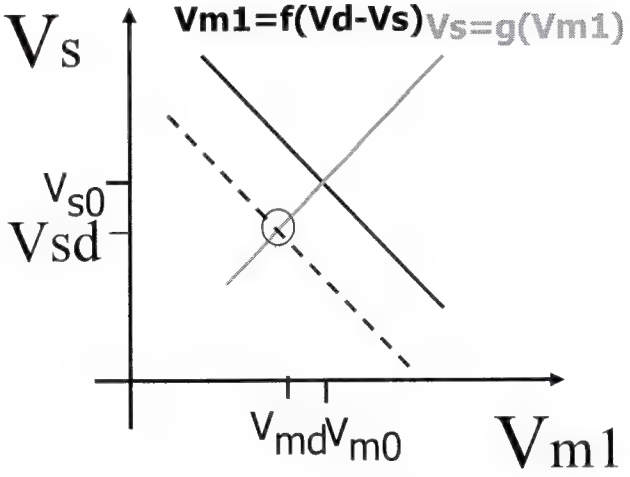




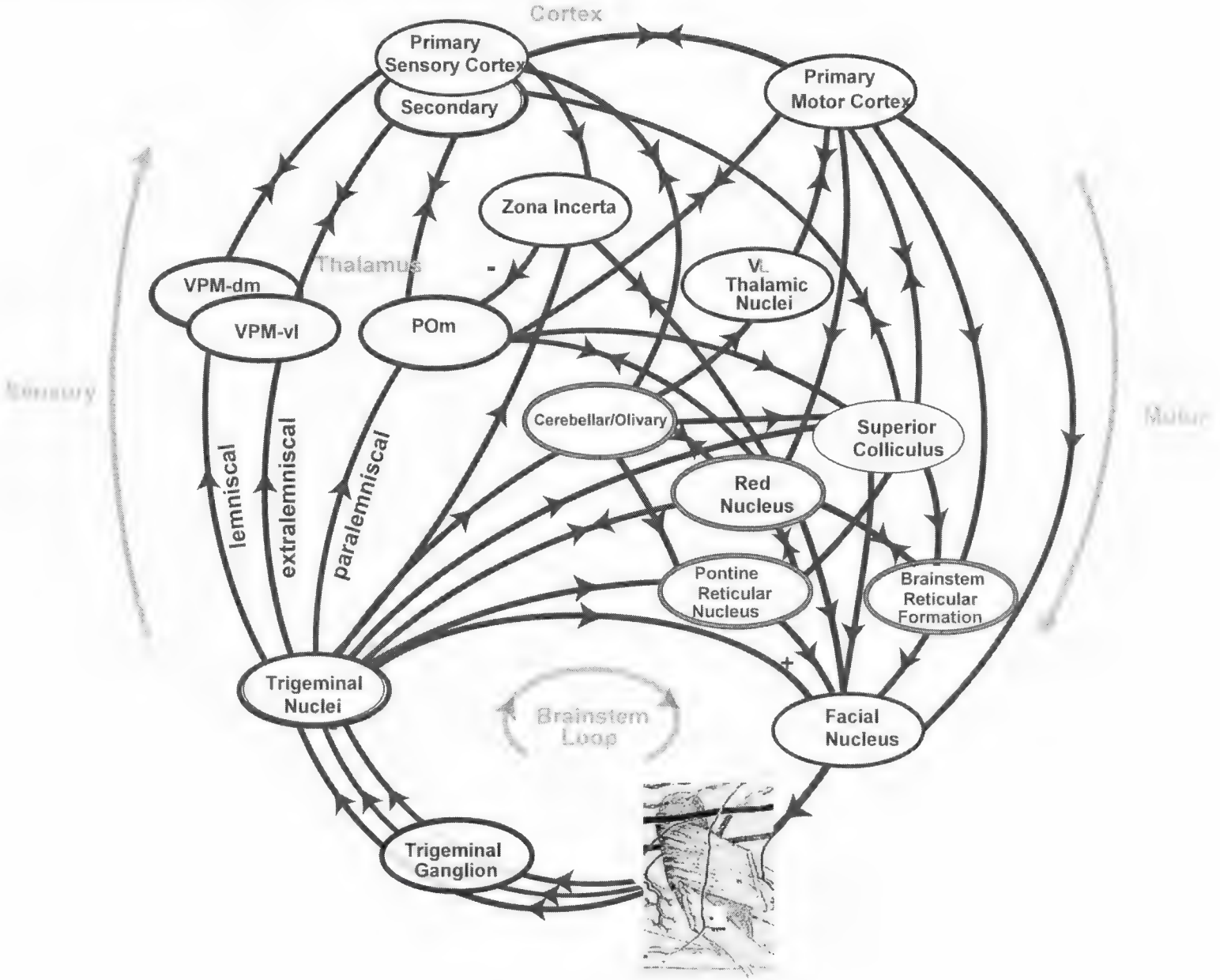
Parallel loops



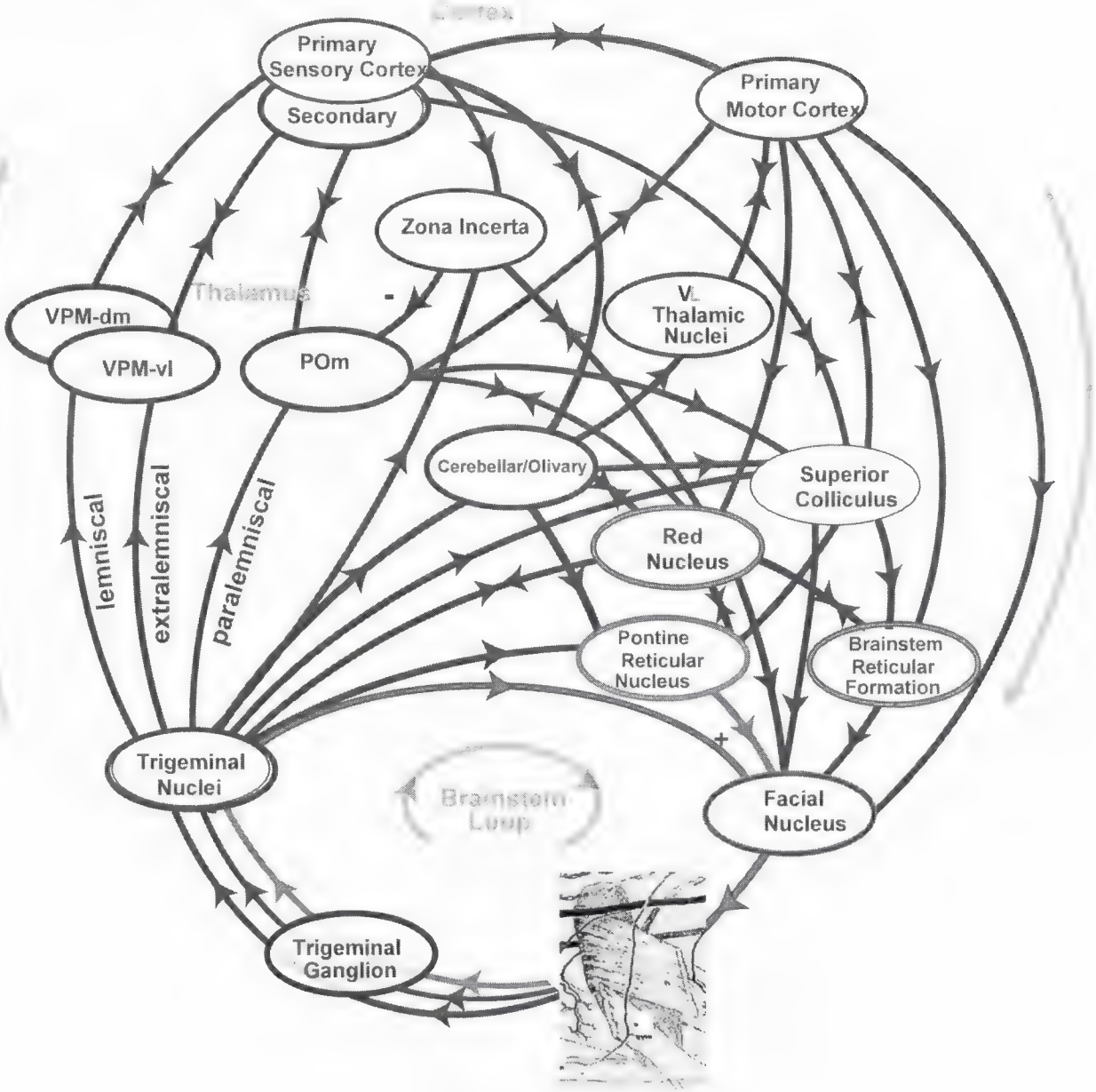




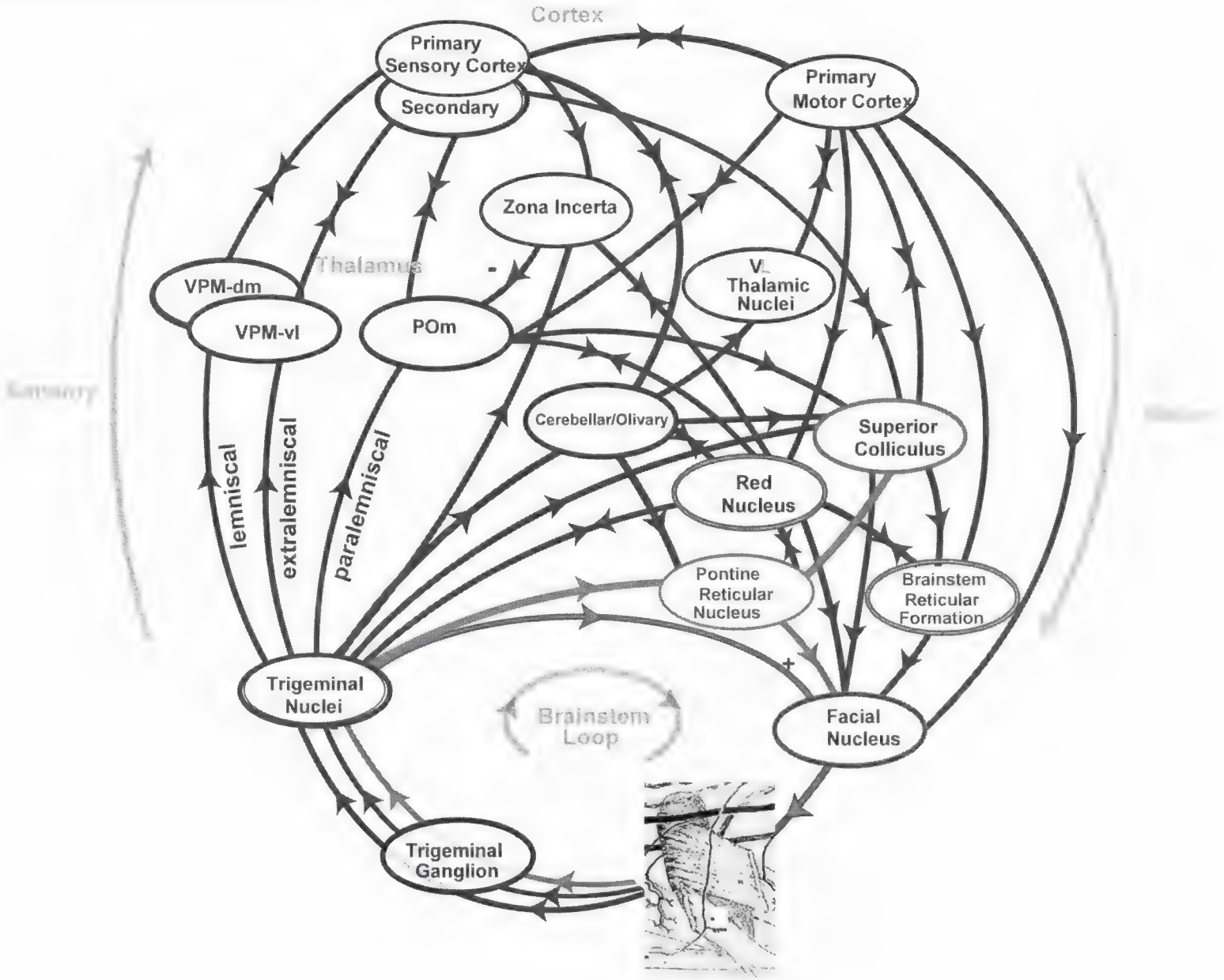
Sensory-motor loops of the vibrissal system



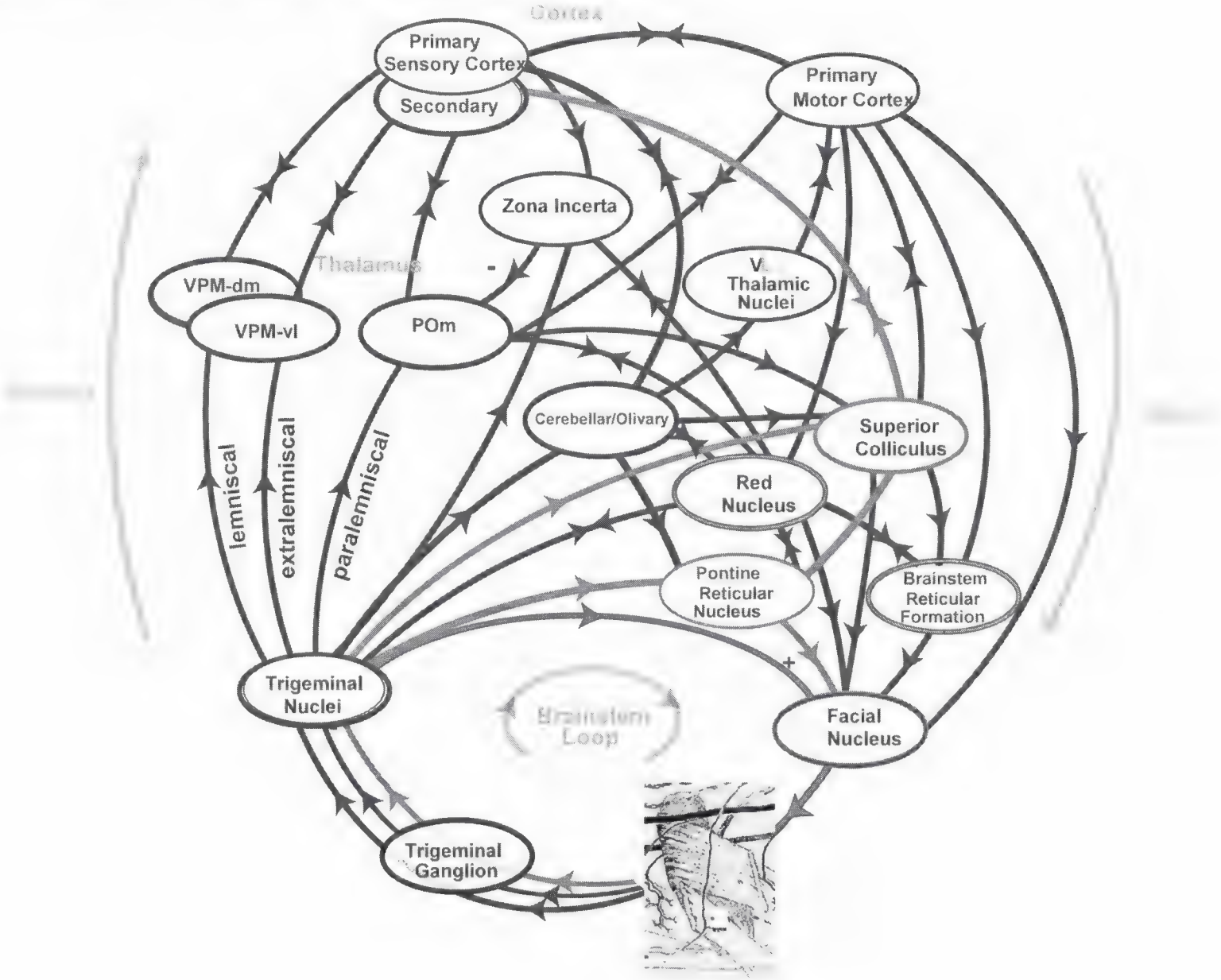
Sensory-motor loops of the vibrissal system



Sensory-motor loops of the vibrissal system



Sensory-motor loops of the vibrissal system



How to study an active system?

- Active mode?

How to study an active system?

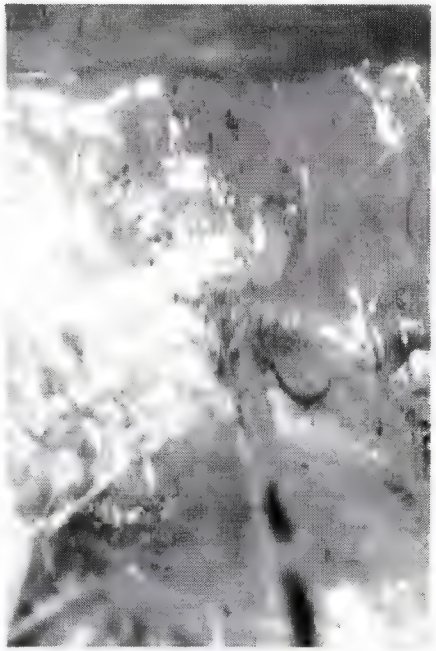
- Active mode?
- Passive stimuli (Newton's 3rd law)?

Passive vs active mechanics

Knarik Bagdasarian

mechanical stimulation

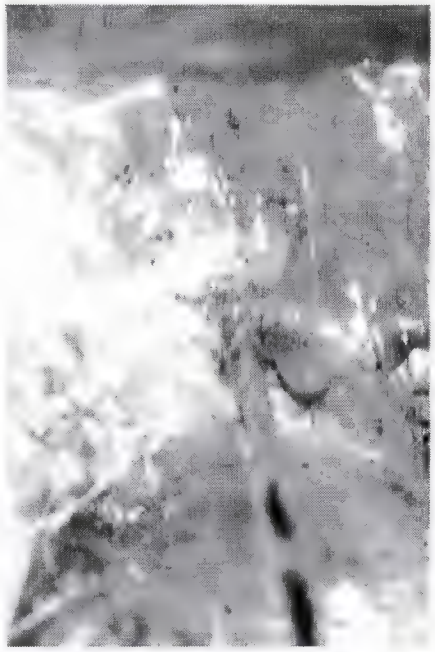
artificial whisking



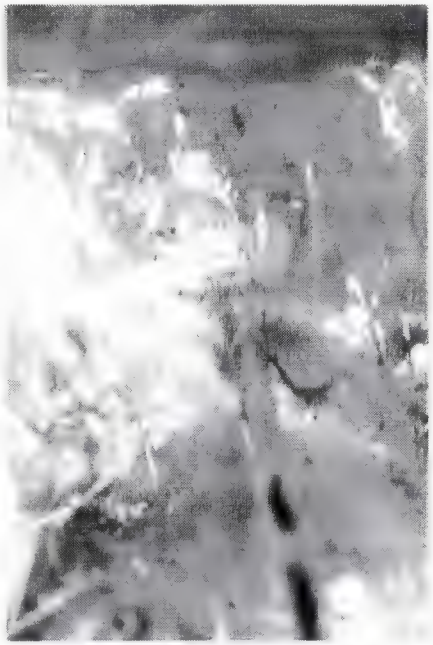
Passive vs active mechanics

Knarik Bagdasarian

artificial whisking

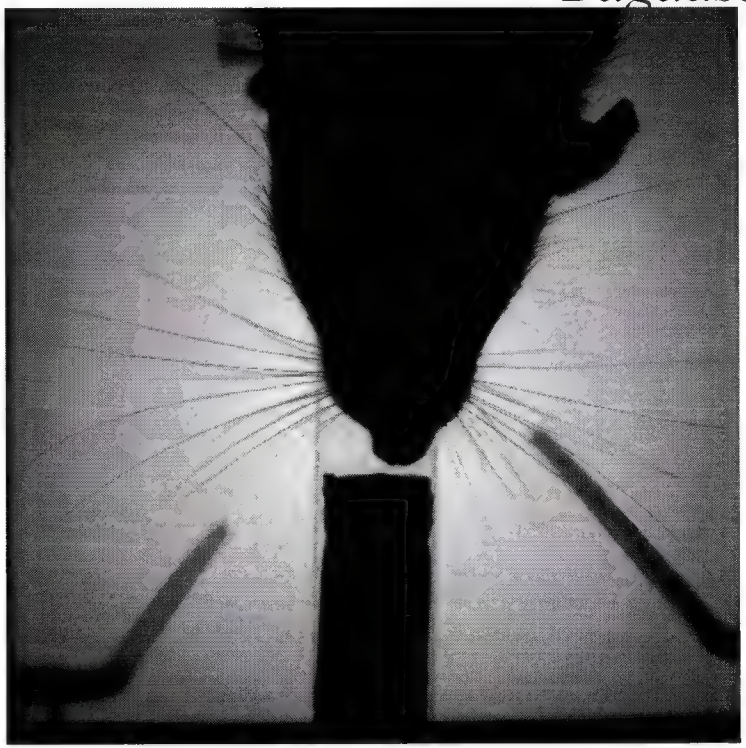


object at 90% (distal)



Artificial whisking

Knarik Bagdasarian



(Szwed, Bagdasarian, Ahissar, *Neuron,* 2003)

How to study an active system?

- Active mode - large variability
- Passive stimuli ≠ active touch

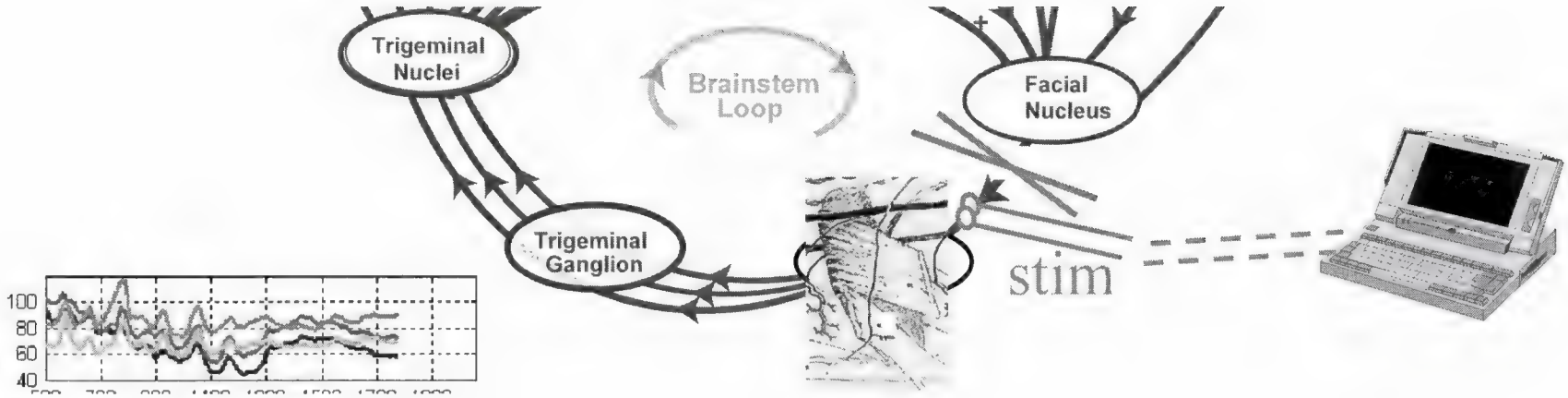
Our research strategy:

Systematic search: artificial whisking in anesthetized rats

Prediction tests and behavioral relevance: Behaving rats

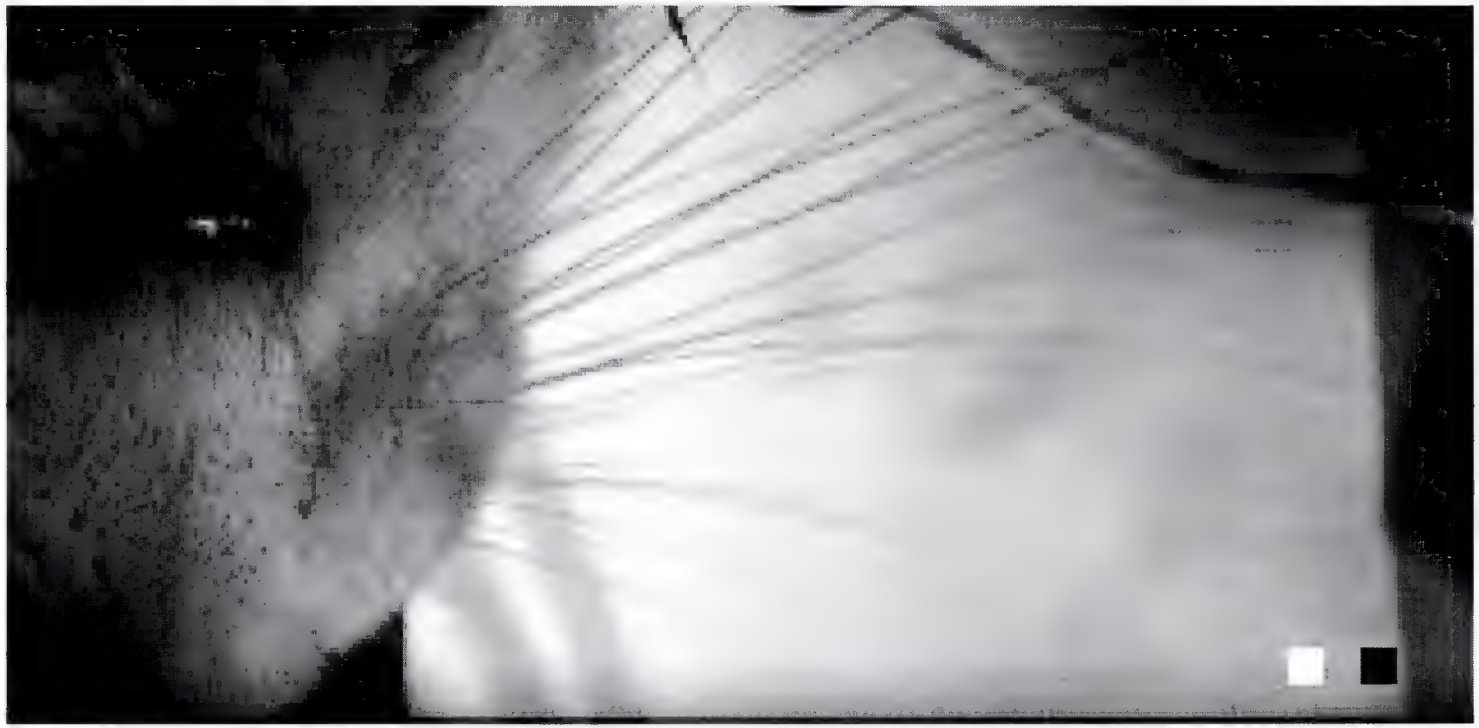
Artificial whisking

Anasthesia



Artificial whisking

Knarik Bagdasarian

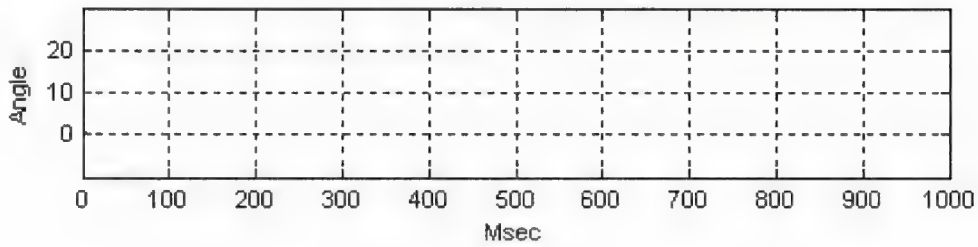


c03_214_rot_1000fps (anest no tracking) compressed

(Szwed, Bagdasarian, Ahissar, *Neuron,* 2003)

Artificial whisking

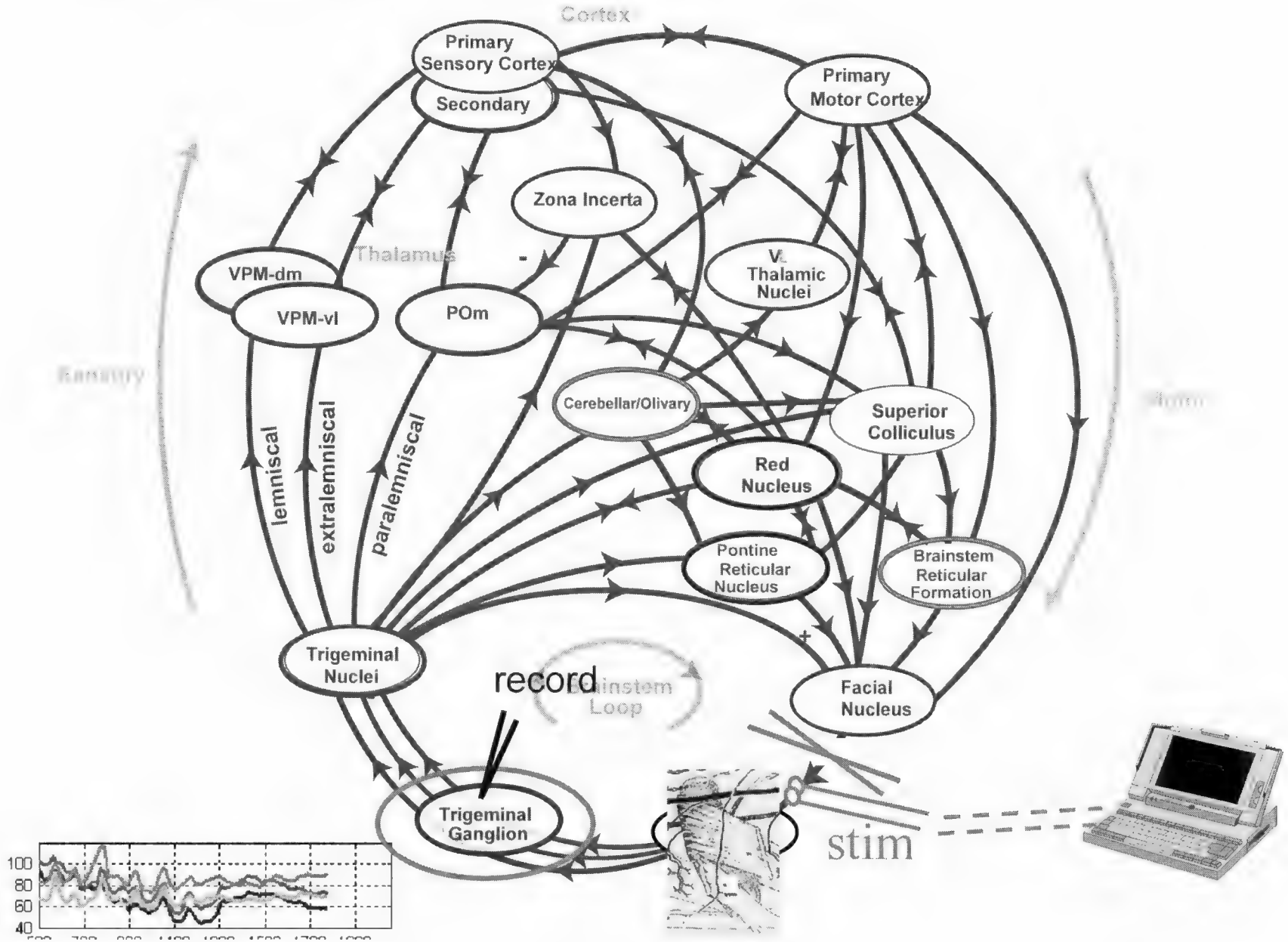
Knarik Bagdasarian



(Szwed, Bagdasarian, Ahissar, *Neuron,* 2003)

What are the sensory inputs?

Artificial whisking



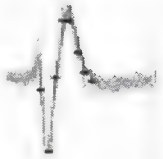
Vibrissa receptors respond differently to active and passive stimuli

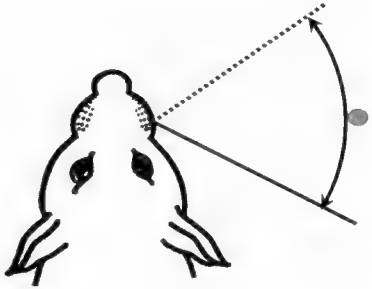
Passive	Active
SA - RA	Whisking
Stimulus direction	Touch
Stimulus intensity	Whisking/Touch

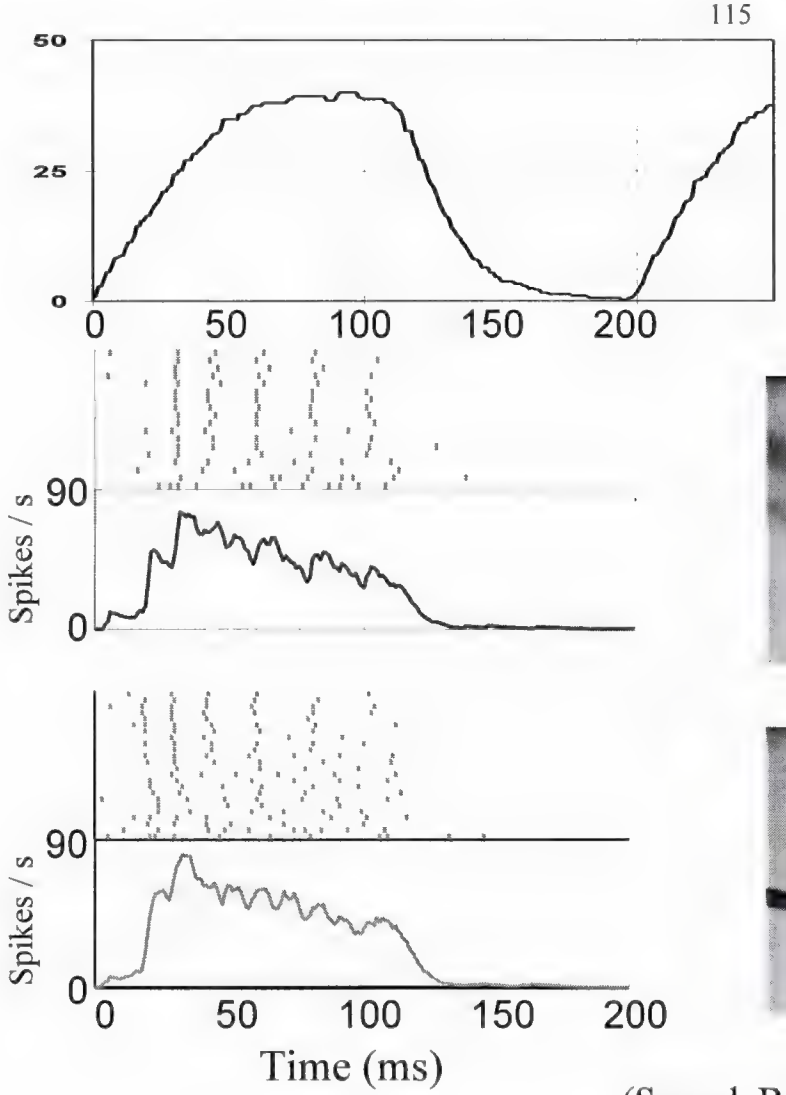
Vibrissa receptors respond differently to active and passive stimuli

Passive	Active
SA - RA	Whisking
Stimulus direction	Touch
Stimulus intensity	Whisking/Touch

A "Whisking cell"

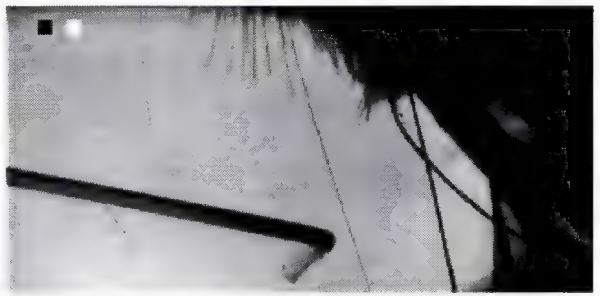






No object

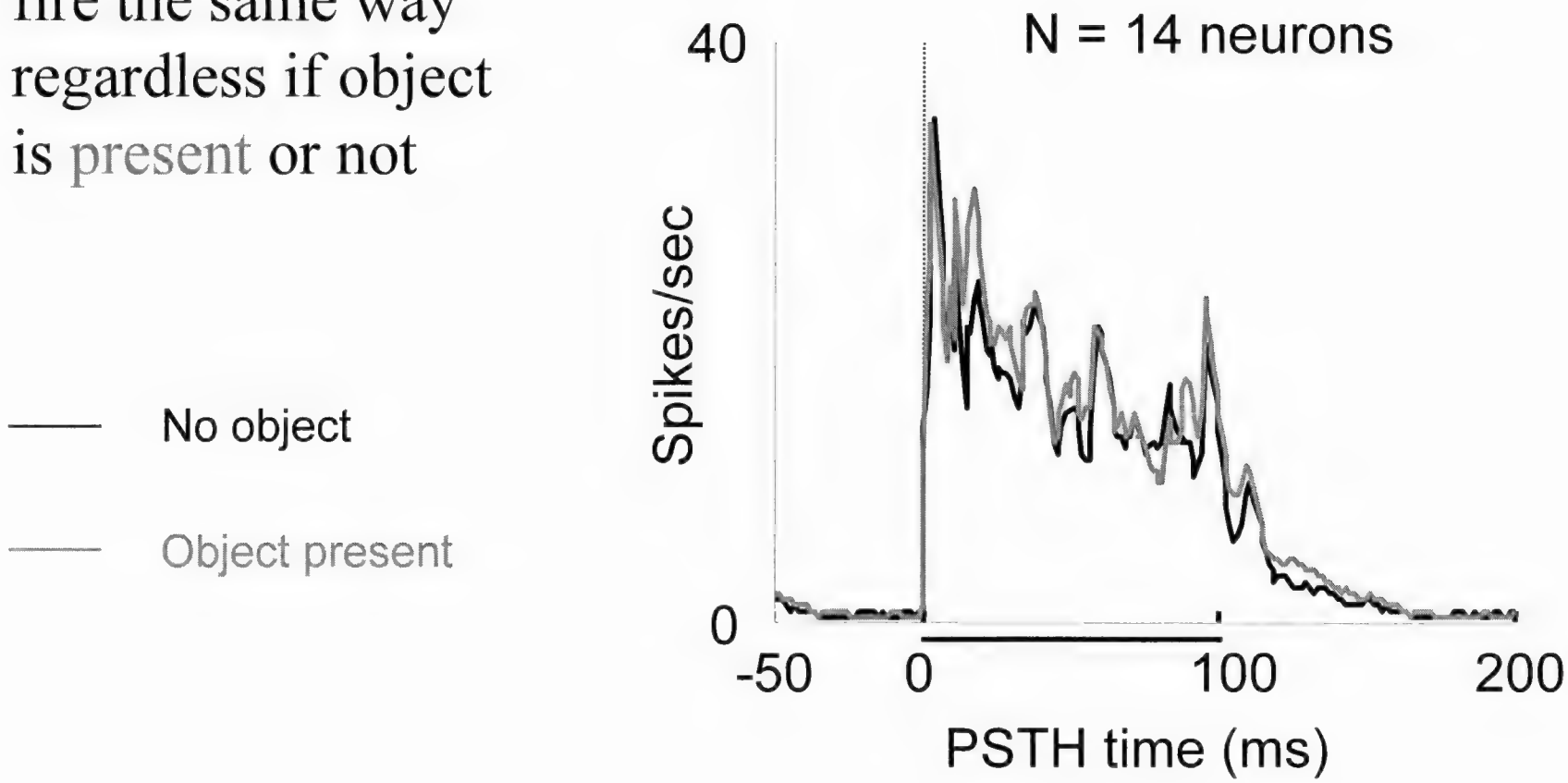
Object



(Szwed, Bagdasarian, Ahissar, *Neuron,* 2003)

Whisking cells
respond only to whisking

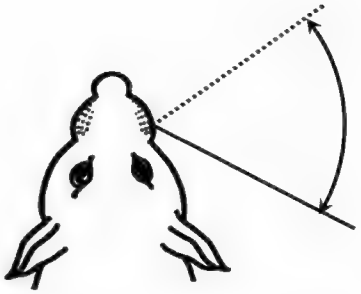
fire the same way
regardless if object
is present or not



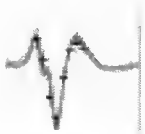
Vibrissa receptors respond differently to active and passive stimuli

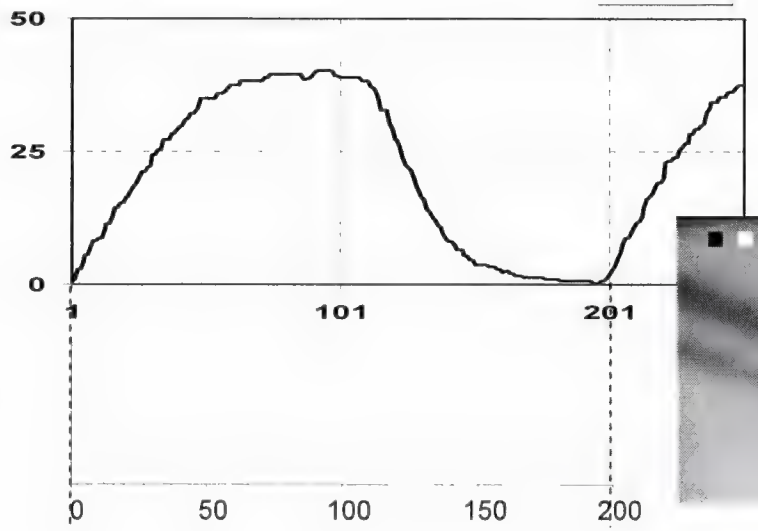
Passive	Active
SA - RA	Whisking
Stimulus direction	Touch
Stimulus intensity	Whisking/Touch

A "Touch cell"

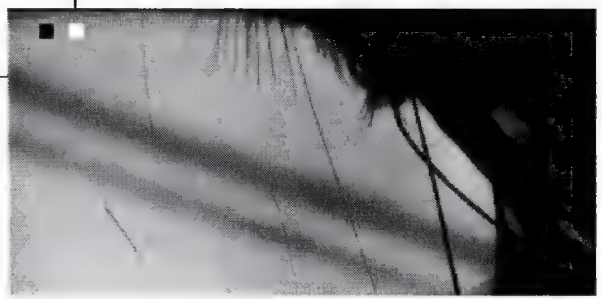


No object



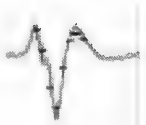


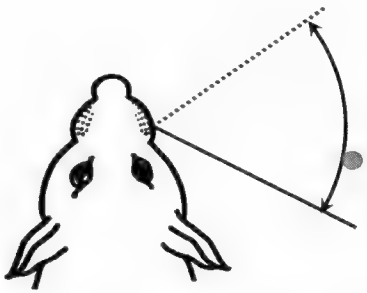
ob43



(Szwed, Bagdasarian, Ahissar, *Neuron,* 2003)

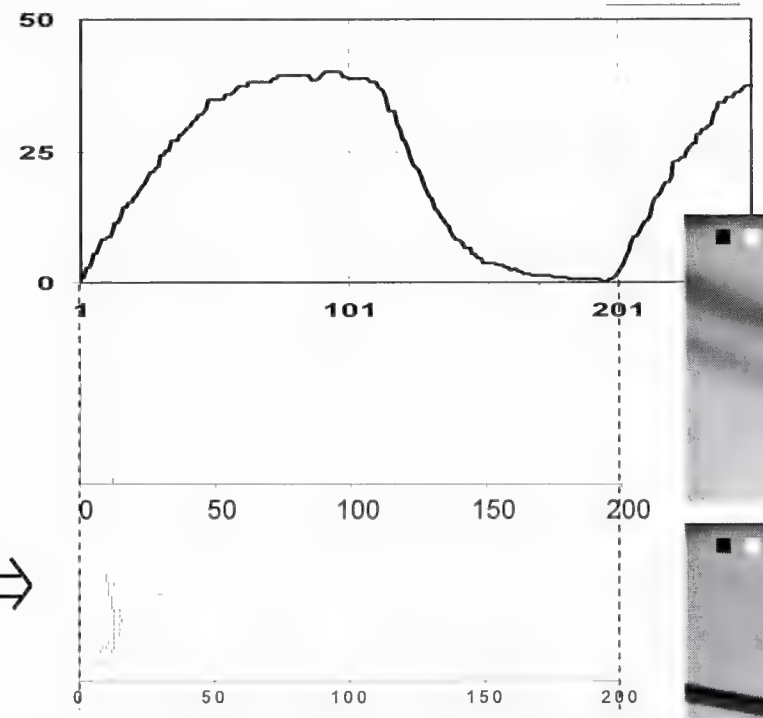
A "Touch cell"

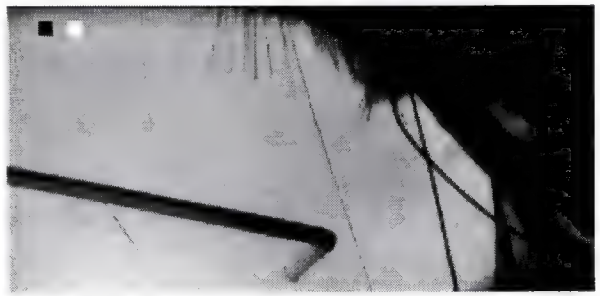




No object

pos 1 (closest) ⇒

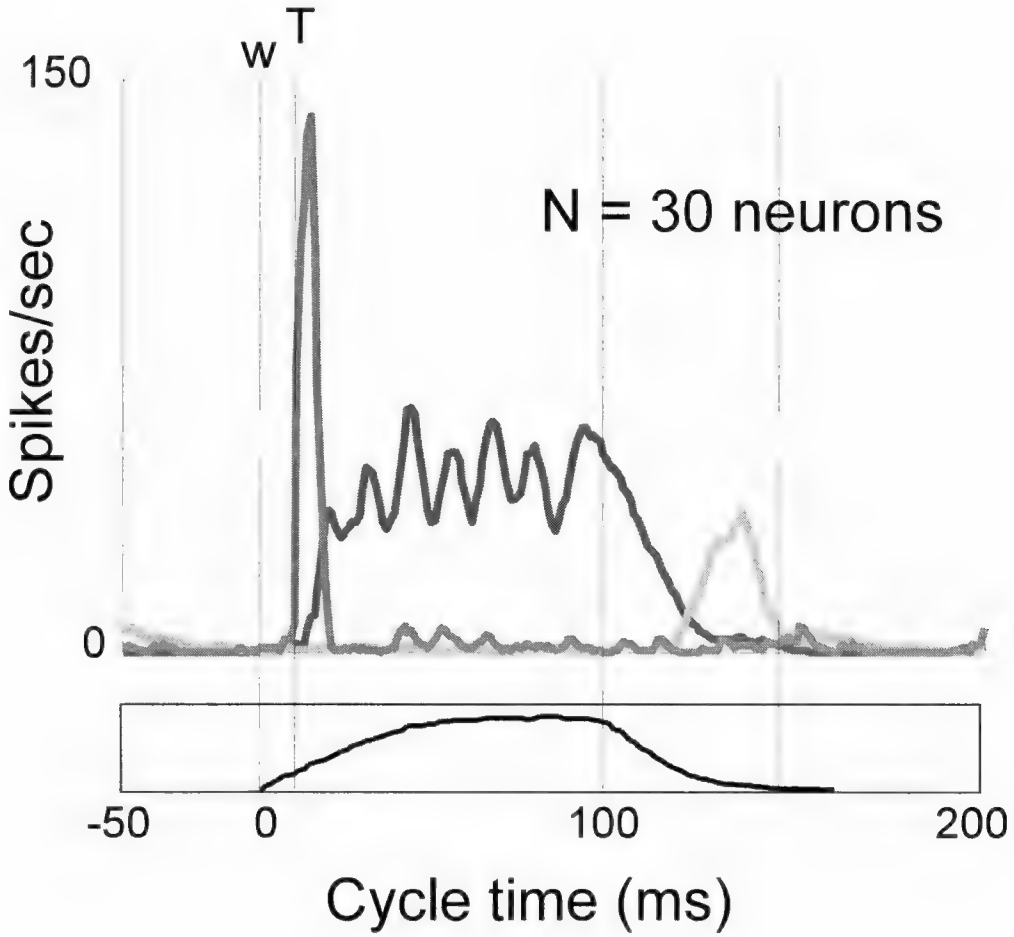




(Szwed, Bagdasarian, Ahissar, *Neuron,* 2003)

Touch cells
respond only to touch

- Contact neurons
- Pressure neurons
- Detach neurons

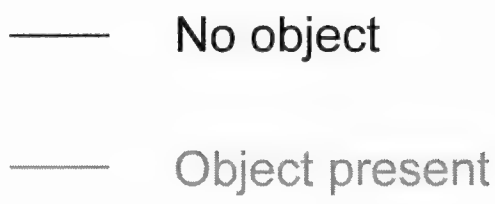


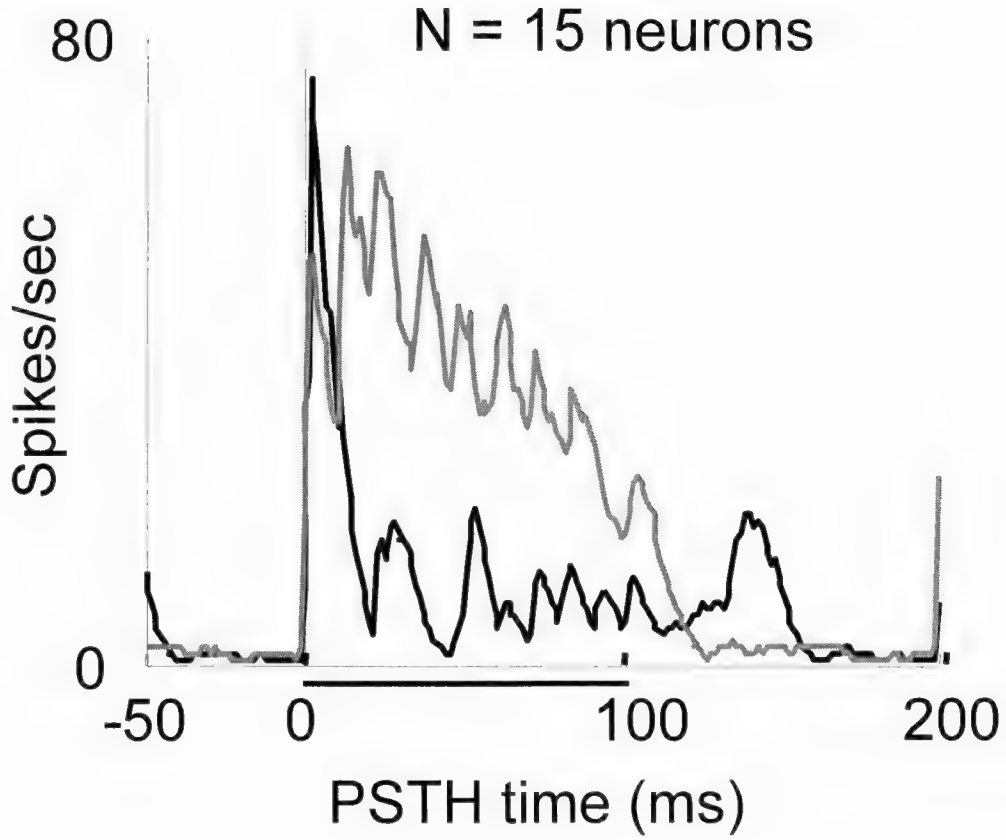
Vibrissa receptors respond differently to active and passive stimuli

Passive	Active
SA - RA	Whisking
Stimulus direction	Touch
Stimulus intensity	Whisking/Touch

Whisking/Touch cells
respond to whisking and touch

fire more spikes when object is present



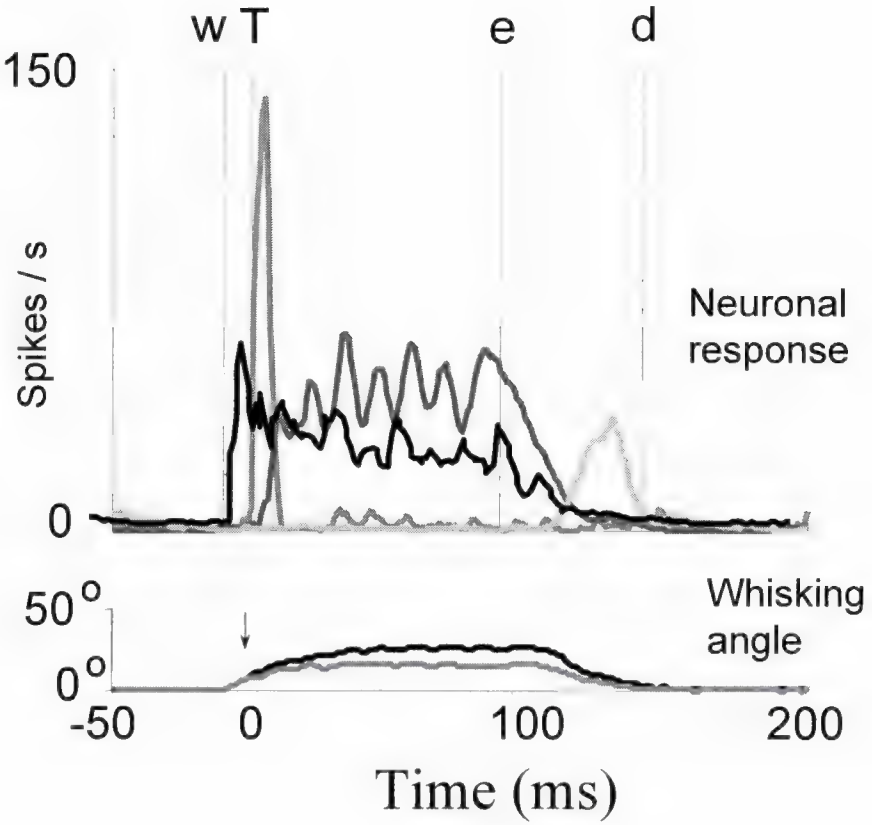


Knarik Bagdasarian

Receptor signals:
Event encoders

Marcin Szwed

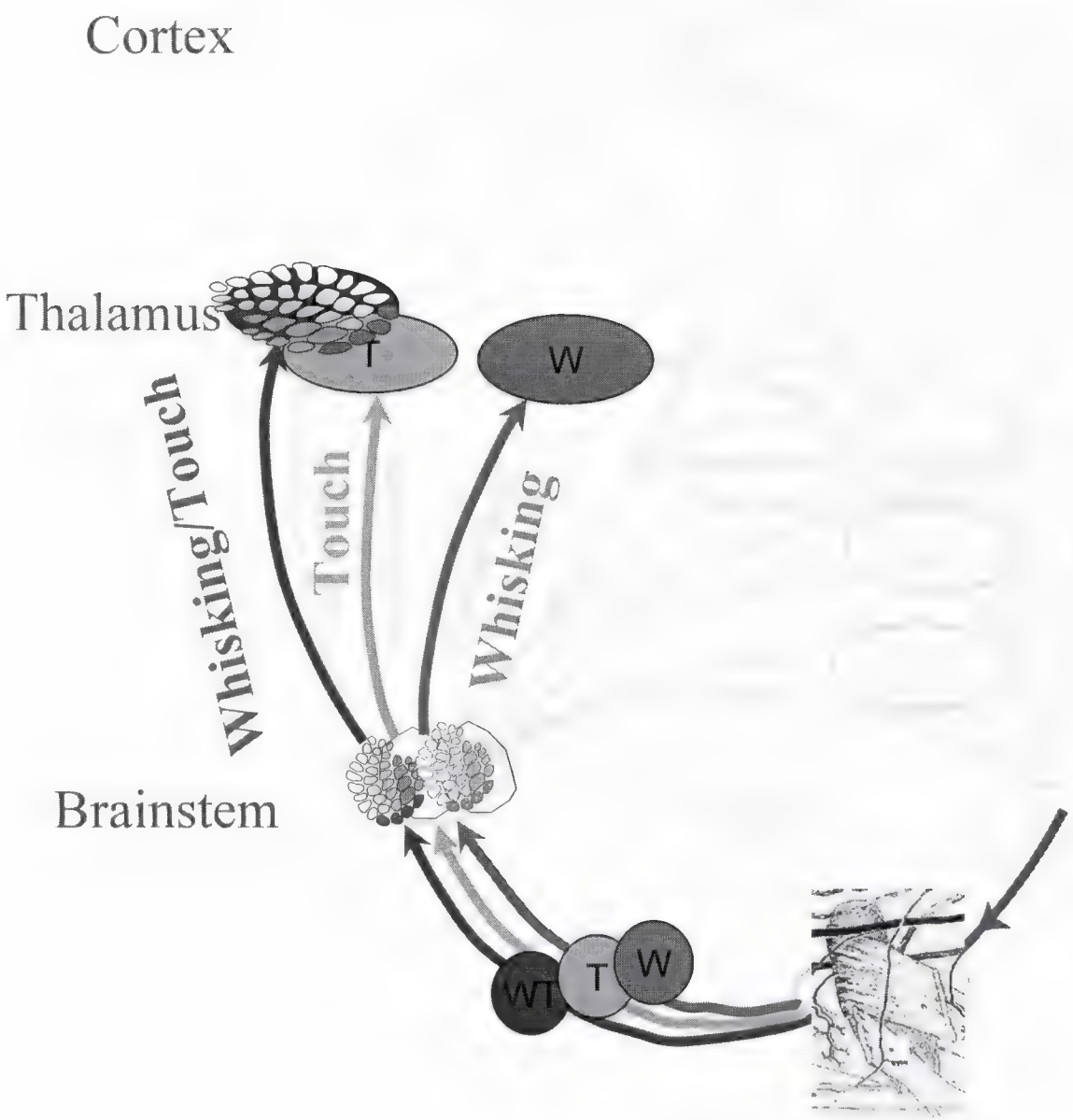
- Whisking ("proprioceptive")
- contact with object
- pressure against object
- detachment from object.
- whisking/touch



(Szwed, Bagdasarian, Ahissar, *Neuron,* 2003)

Afferent flow of sensory signals

Afferent information

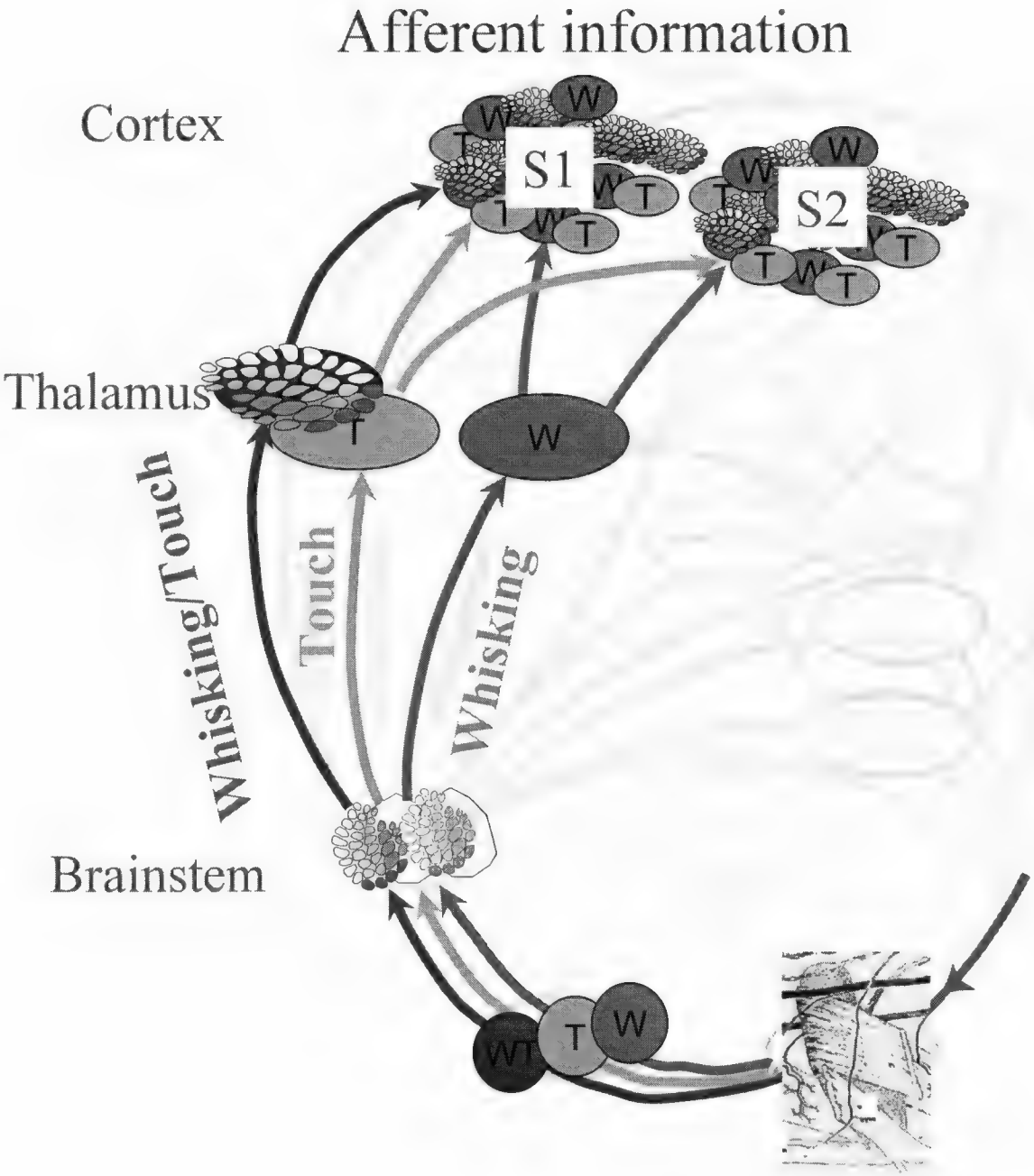


Chunxiu Yu

Sebastian Haidarliu

Naama Rubin

Dori Derdikman

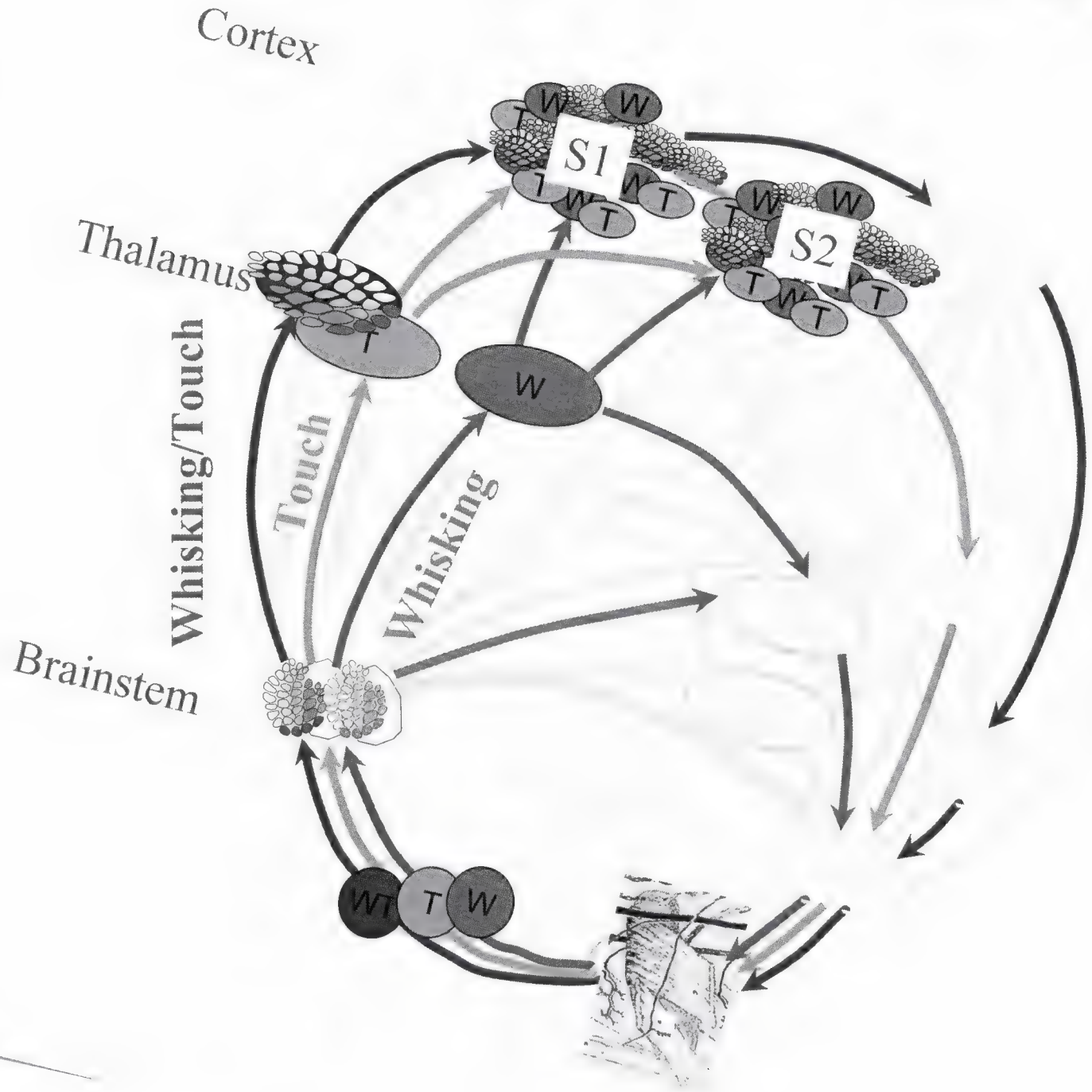


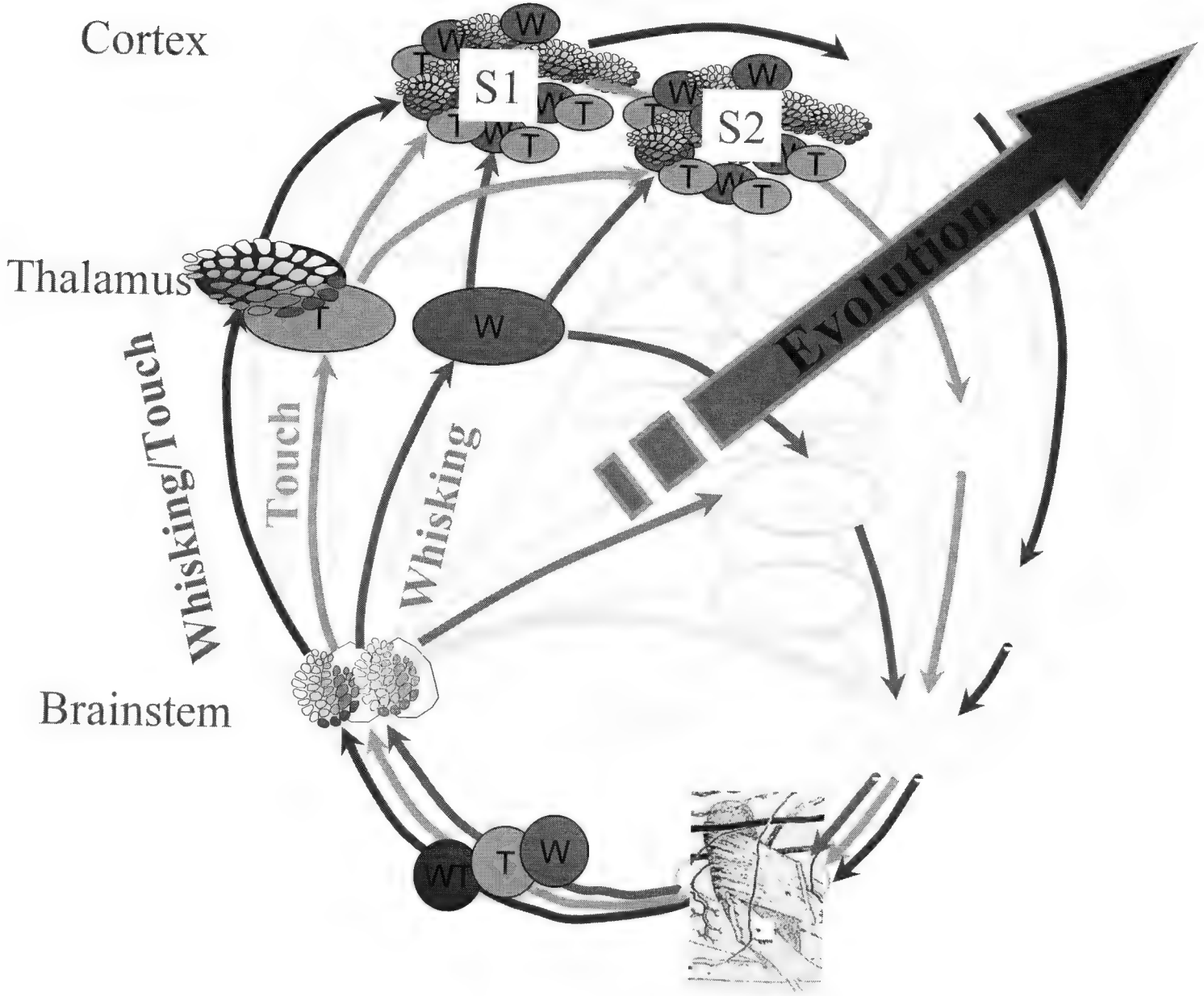
Chunxiu Yu

Sebastian Haidarliu

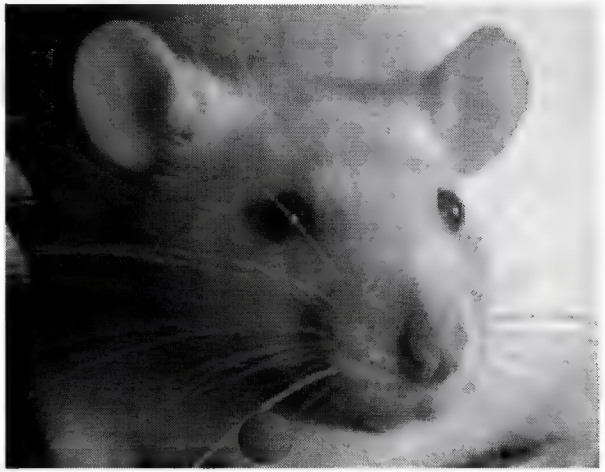
Naama Rubin

Dori Derdikman


Cortex
S1
S2
Thalamus
Whisking/Touch
Touch
Whisking
Brainstem
W
T


Cortex
S1
S2
Thalamus
Brainstem
Whisking/Touch
Touch
Whisking
Evolution
W
T
WT

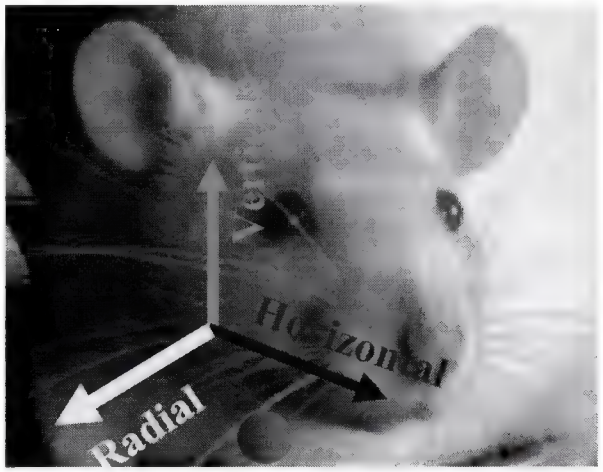
How rats localize objects?



How rats localize objects?

Coordinates of object location

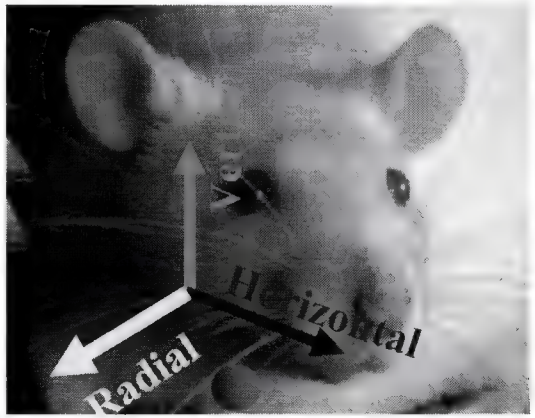
Head-centered



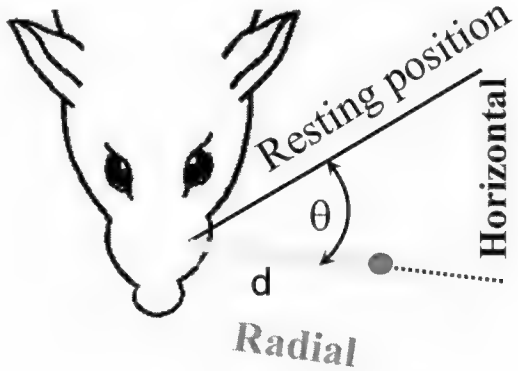
How rats localize objects?

Coordinates of object location

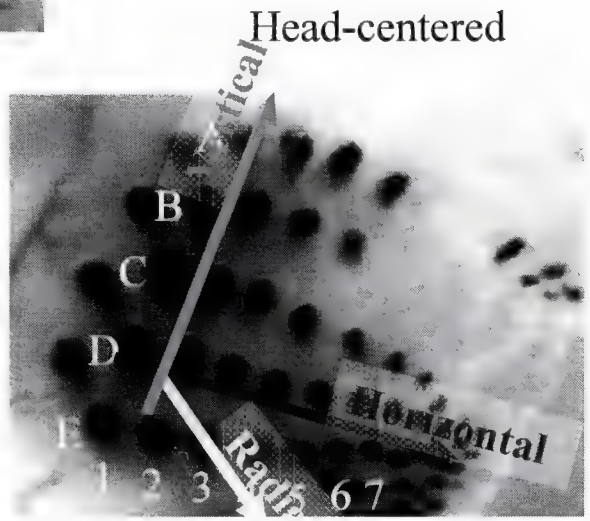
Head-centered



Whisker-centered

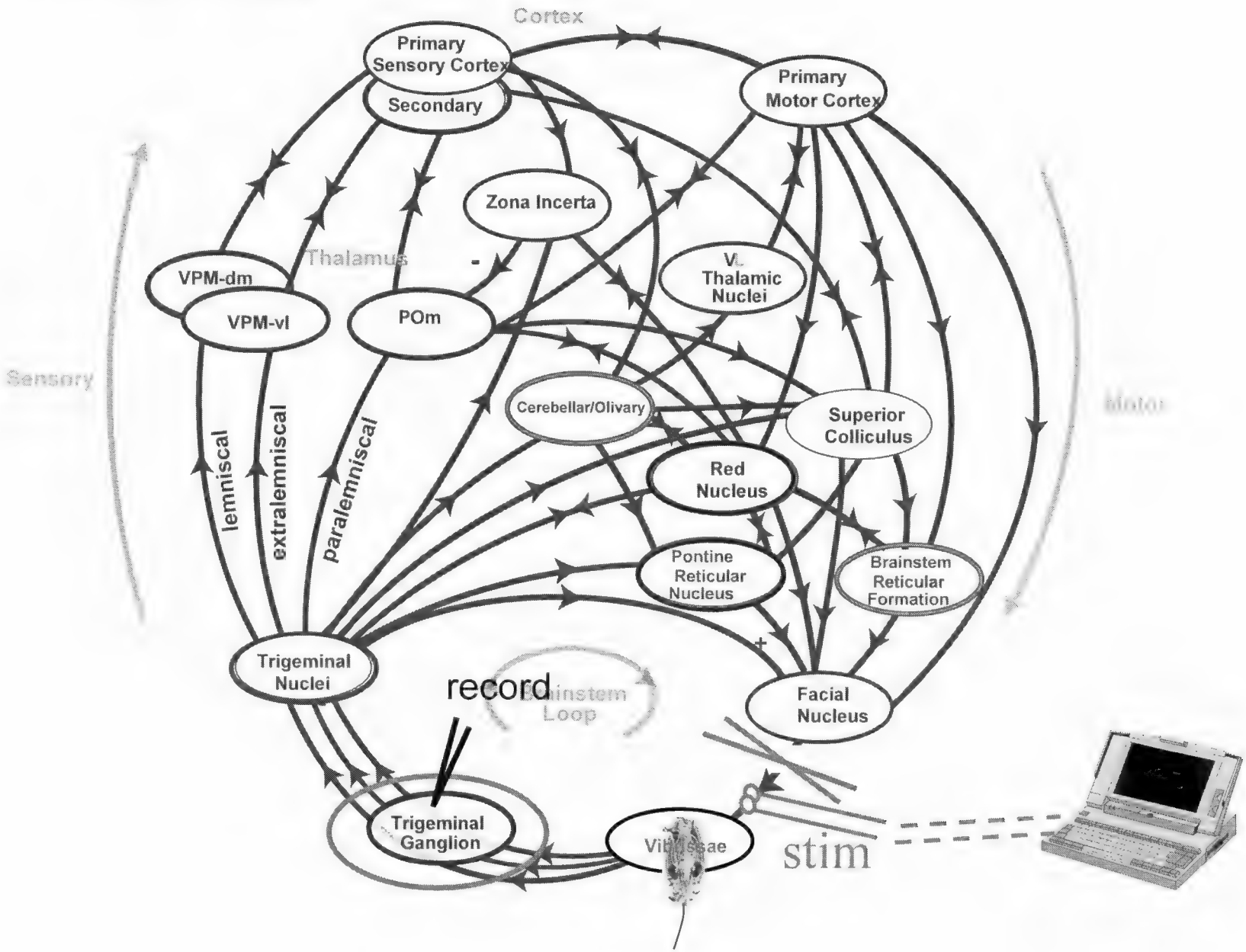


Head-centered



Neuronal data
(artificial whisking in anesthetized rats)

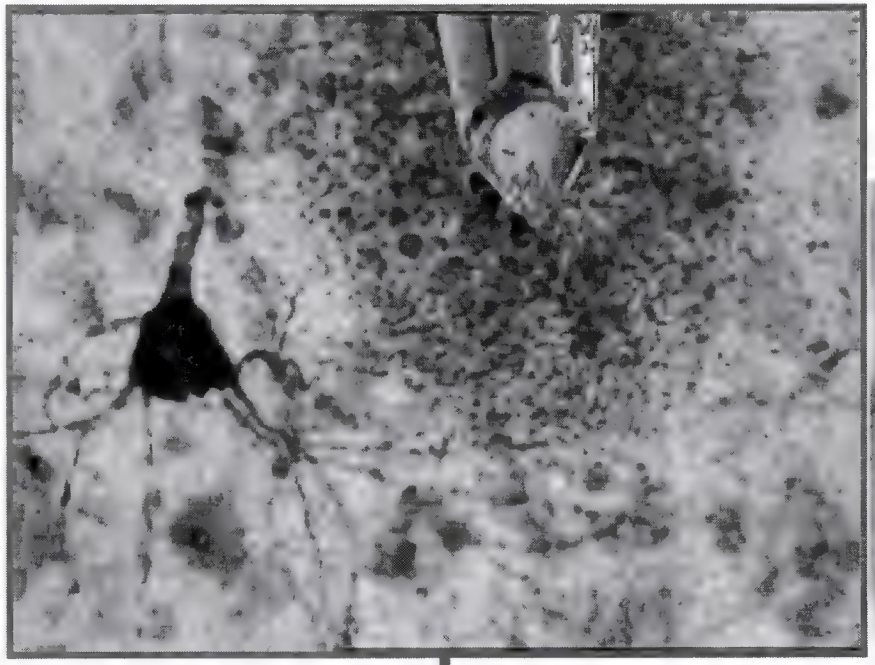
Artificial whisking

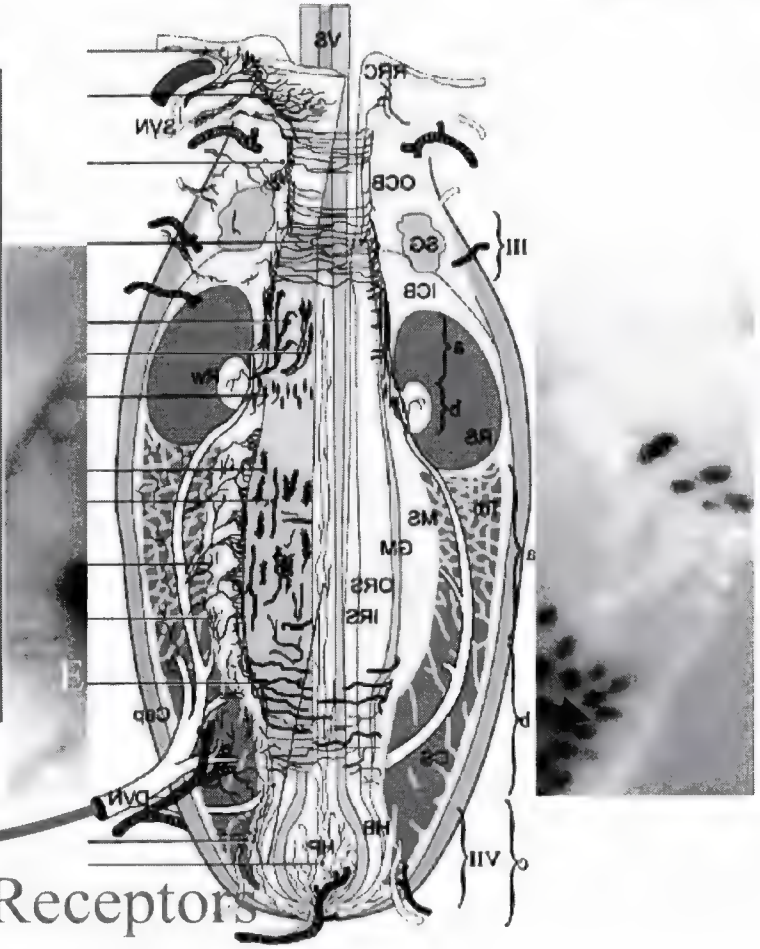


Knarik Bagdasarian

Recording from the trigeminal ganglion

Marcin Szwed

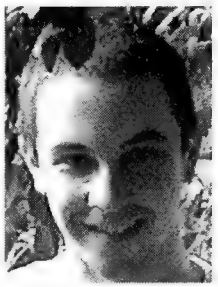




Brain

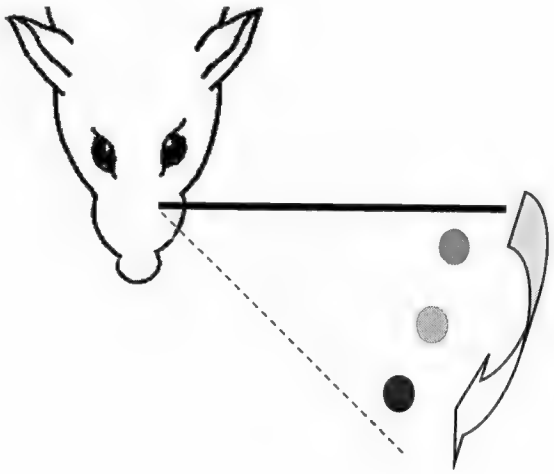
Receptors

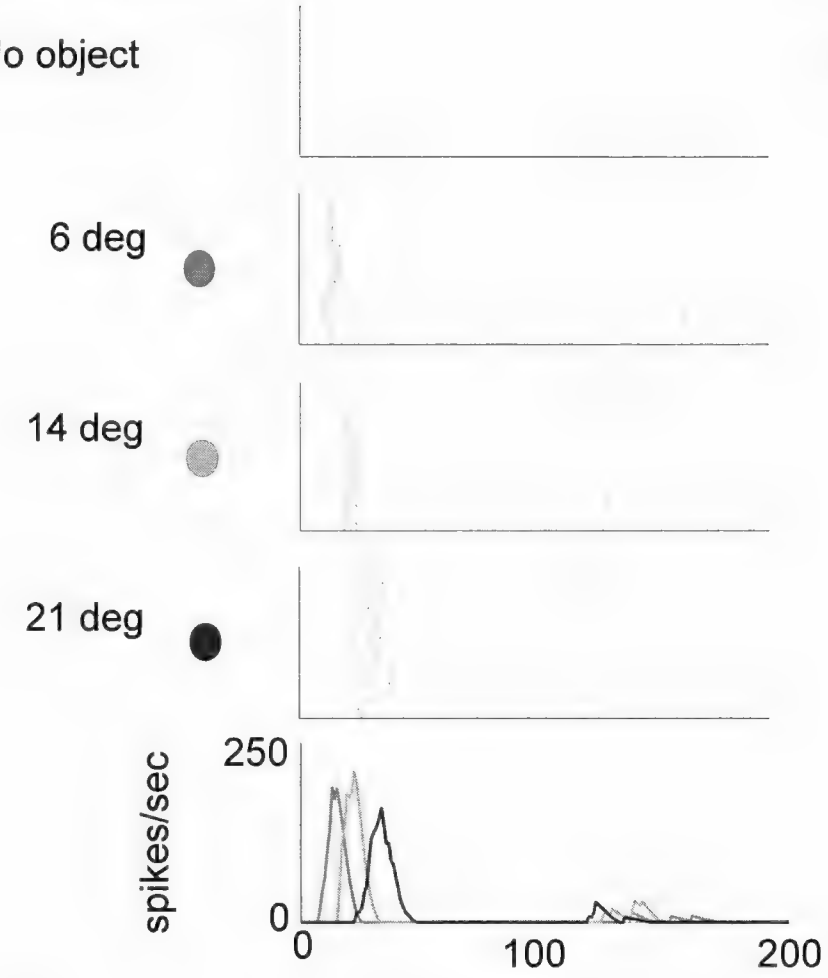
The horizontal coordinate (azimuth) is encoded by time



Knarik Bagdasarian

Marcin Szwed



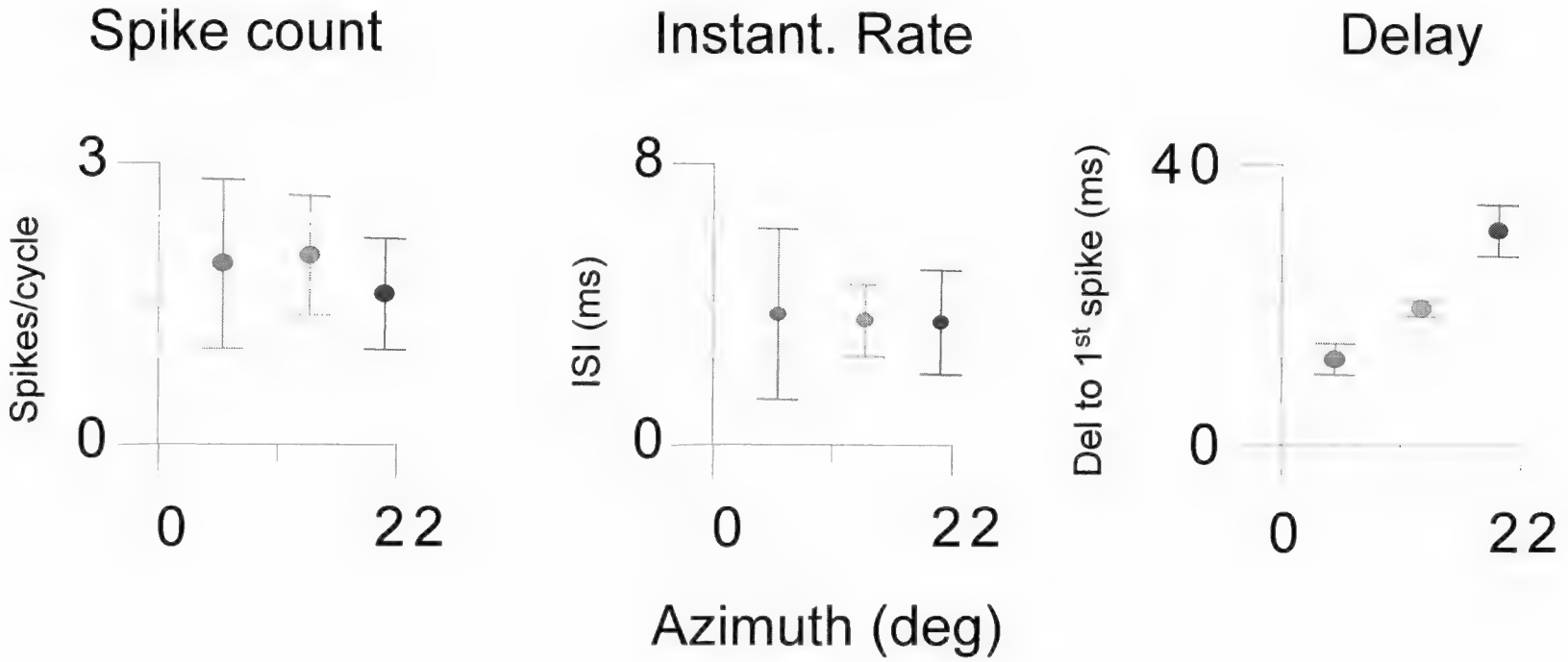


(Szwed, Bagdasarian, Ahissar, *Neuron,* 2003)

Knarik Bagdasarian

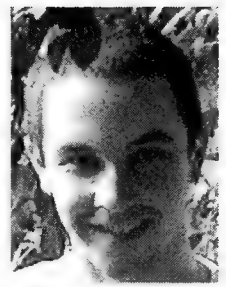
Coding reliability of a Single Contact cell

Marcin Szwed

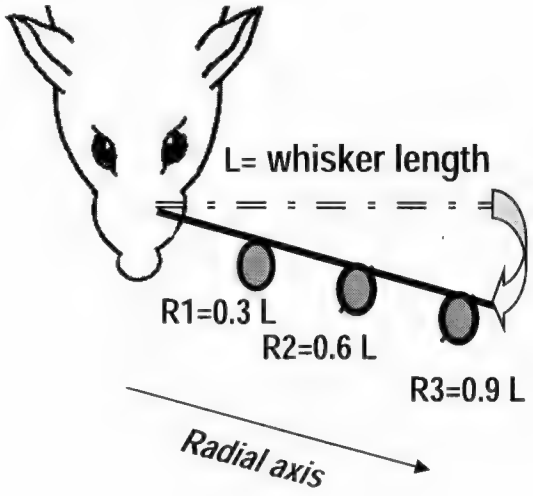


Knarik Bagdasarian

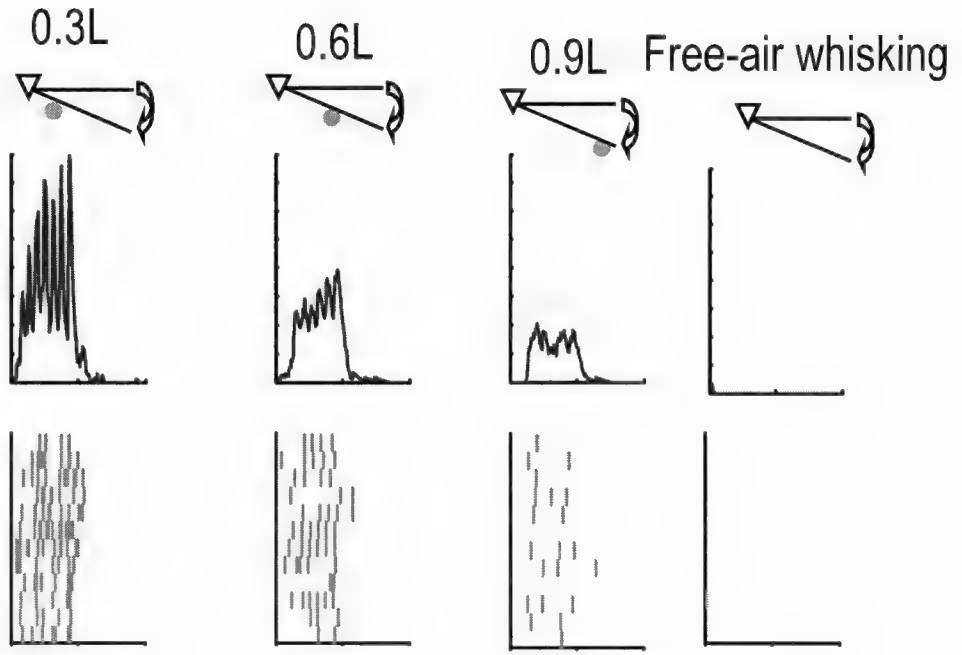
The radial coordinate is encoded by firing-rate



Marcin Szwed



"Electrical" whisking



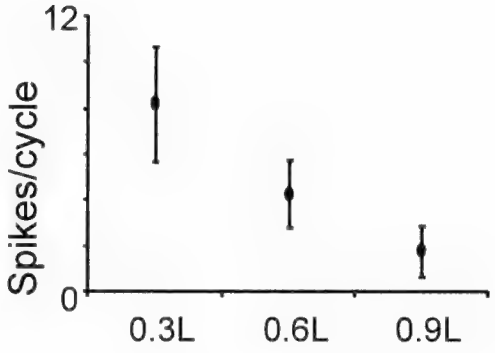
(Szwed et al., *J Neurophysiol,* 2006)

Knarik Bagdasarian

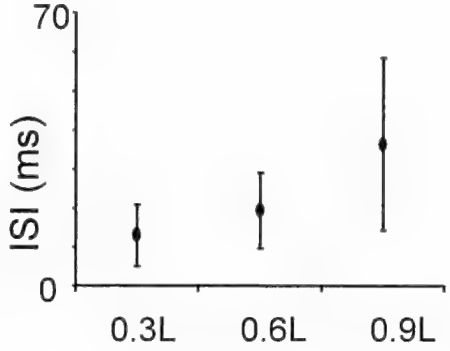
Coding reliability of a Single Pressure cell

Marcin Szwed

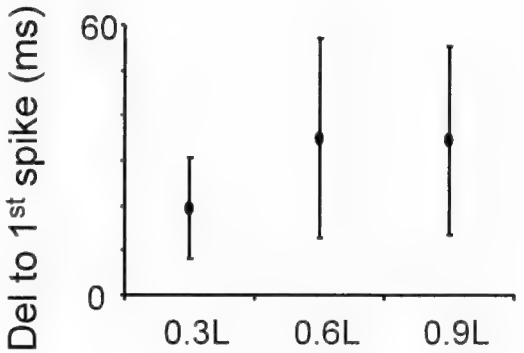
Spike count



Instant. Rate

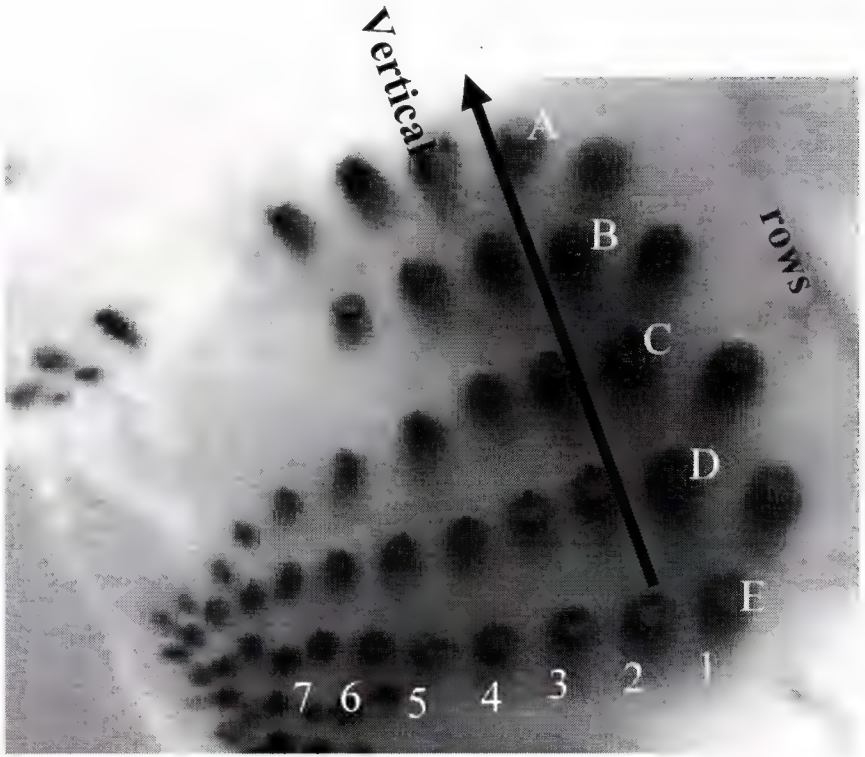


Delay



Radial distance (fraction of whisker length)

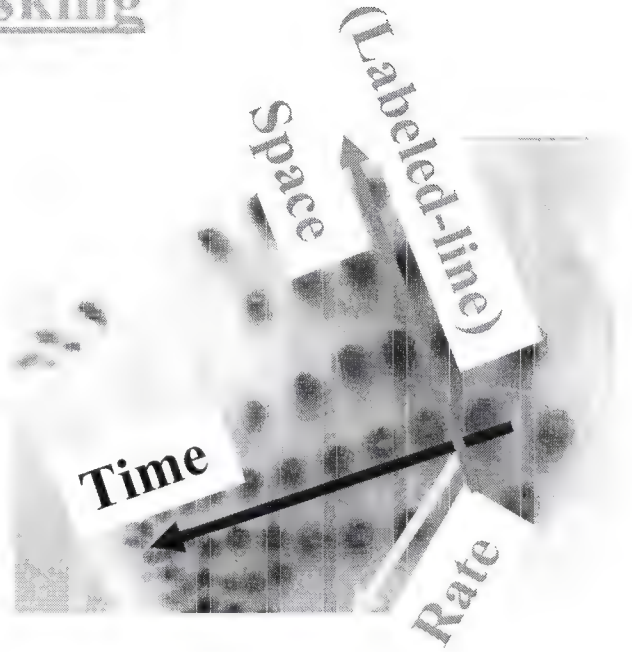
The vertical coordinate (elevation) is encoded by space (labeled line)



Encoding of object location

Implications from artificial whisking

- Vertical object position is encoded by space
- Horizontal object position is encoded by time
- Radial object position is encoded by rate

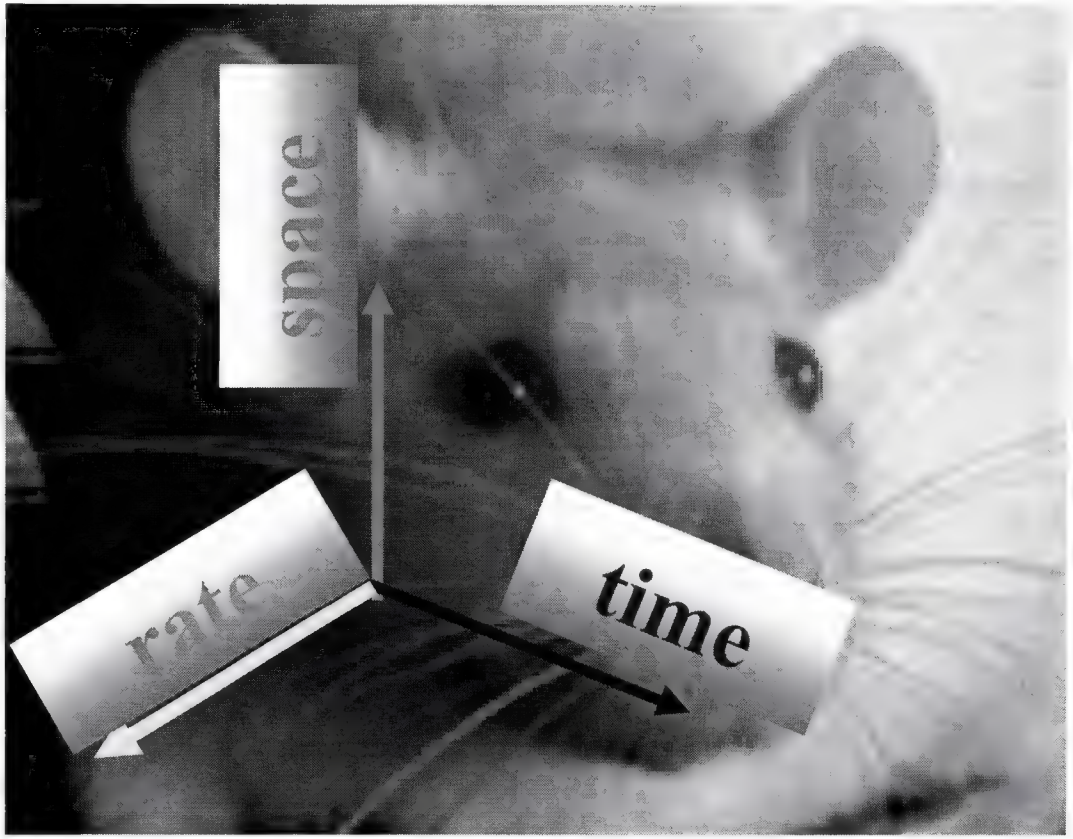


ex

Knarik Bagdasarian

Object location coding

Marcin Szwed



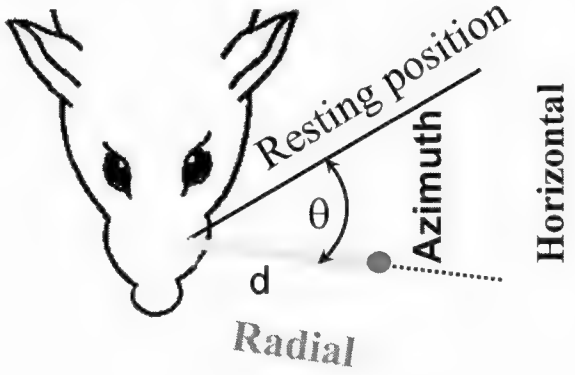
- Vertical by space
- Horizontal by time
- Radial by rate

Consistency with rat behavior

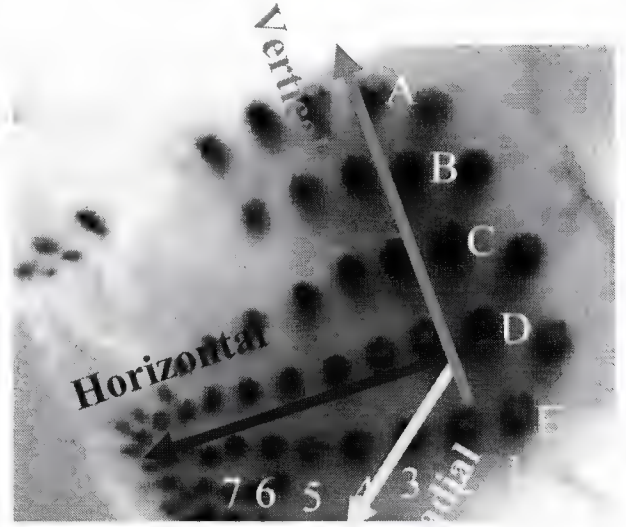
Coordinates of object location

Horizontal

Whisker-centered



Head-centered



Possible coding of horizontal location

Spatial code?

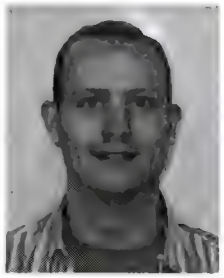
Identity code? (labeled line)

Interpolation code?

Rate code?

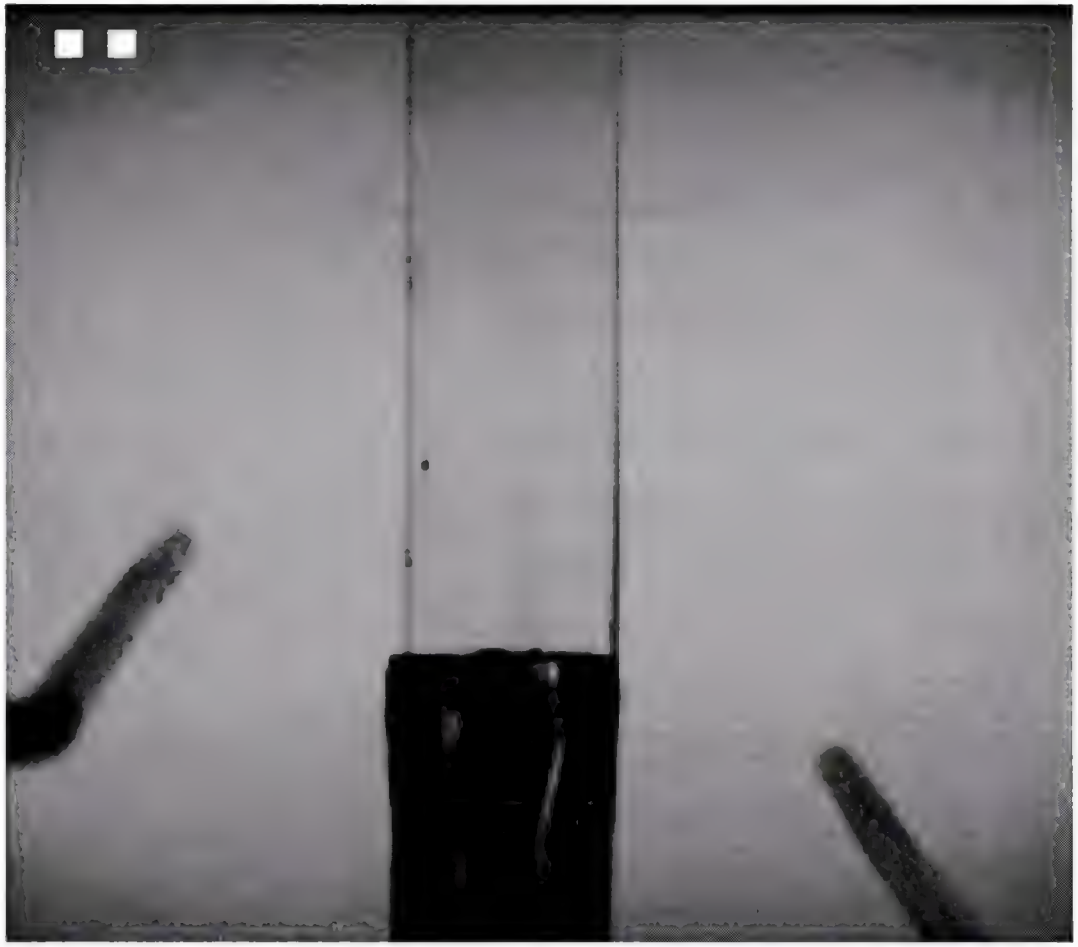
Temporal code?

proprioceptive?



Per Knutsen

Horizontal object localization

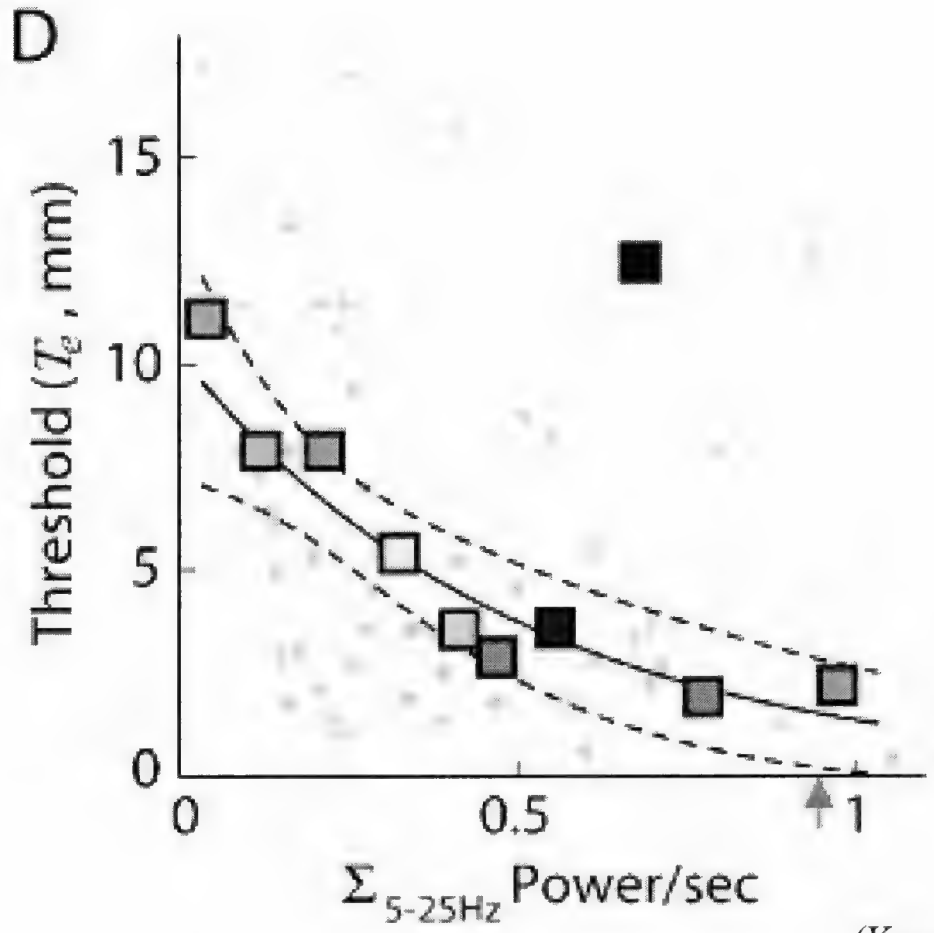


Maciej Pietr

137_271003_1_37_B_50fps (task all whiskers) uncompressed

(Knutsen, Pietr, Ahissar, *J Neurosci,* 2006)

Horizontal localization resolved via whisking

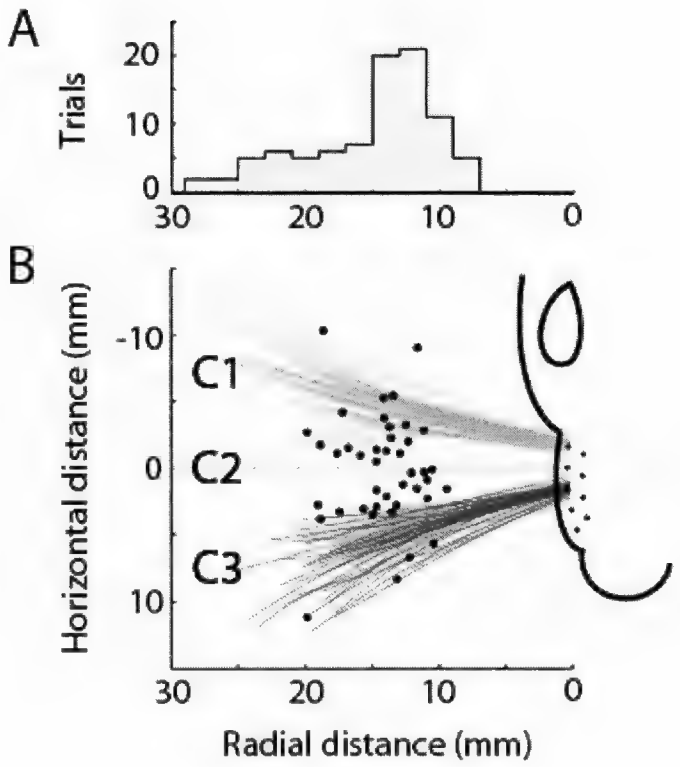


(Knutsen et al, *J Neurosci,* 2006)

Per Knutsen

Localization hyperacuity

Maciej Pietr



(Knutsen, Pietr, Ahissar, *J Neurosci,* 2006)

Possible coding of horizontal location

Spatial code?

Hyperacuity ==> ~~Identity code?~~ ~~(labeled line)~~

Interpolation code?

Rate code?

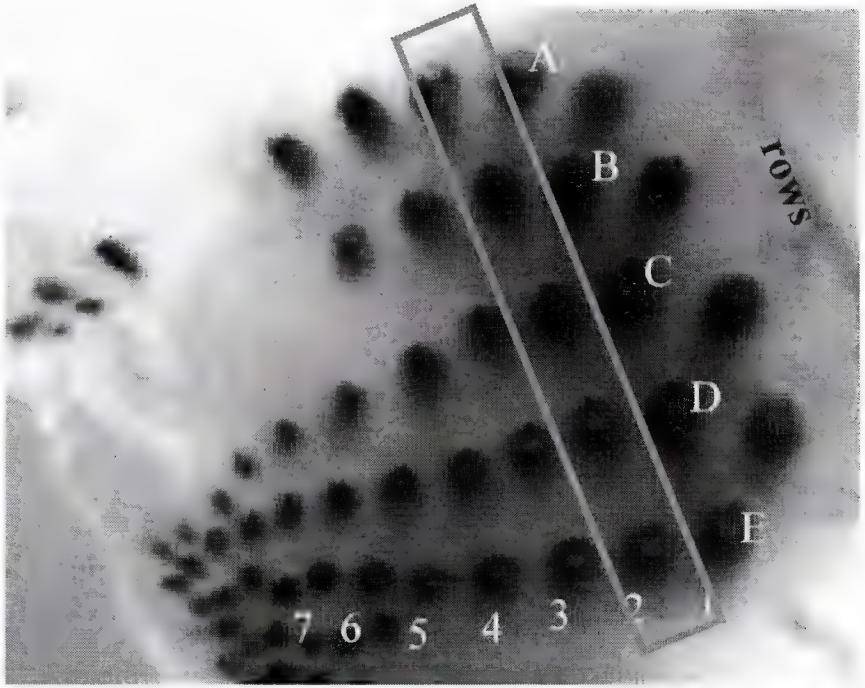
Temporal code?

proprioceptive?

Per Knutsen

Effect of spatial configuration

Maciej Pietr



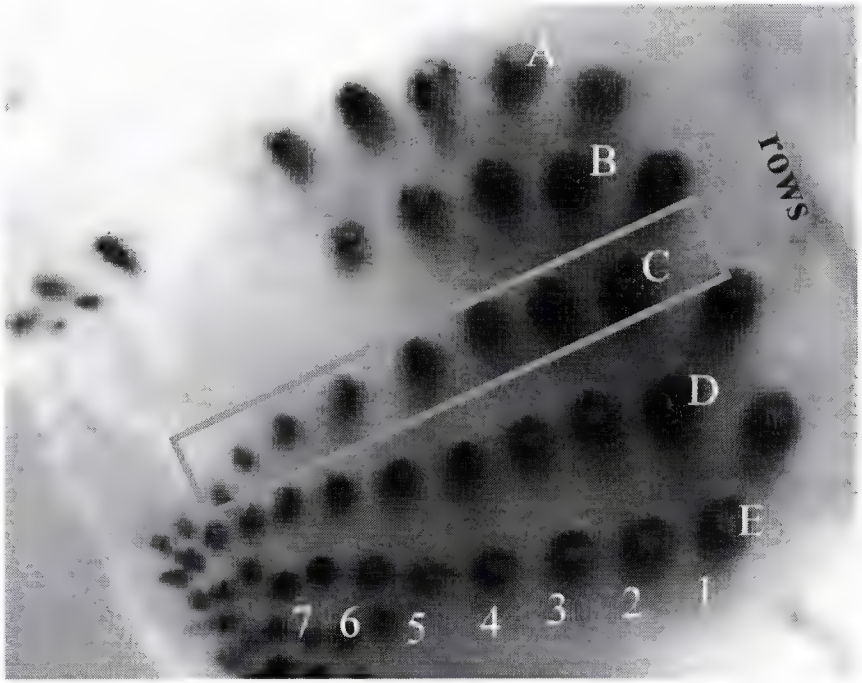
arcs

(Knutsen, Pietr, Ahissar, *J Neurosci,* 2006)

Per Knutsen

Effect of spatial configuration

Maciej Pietr

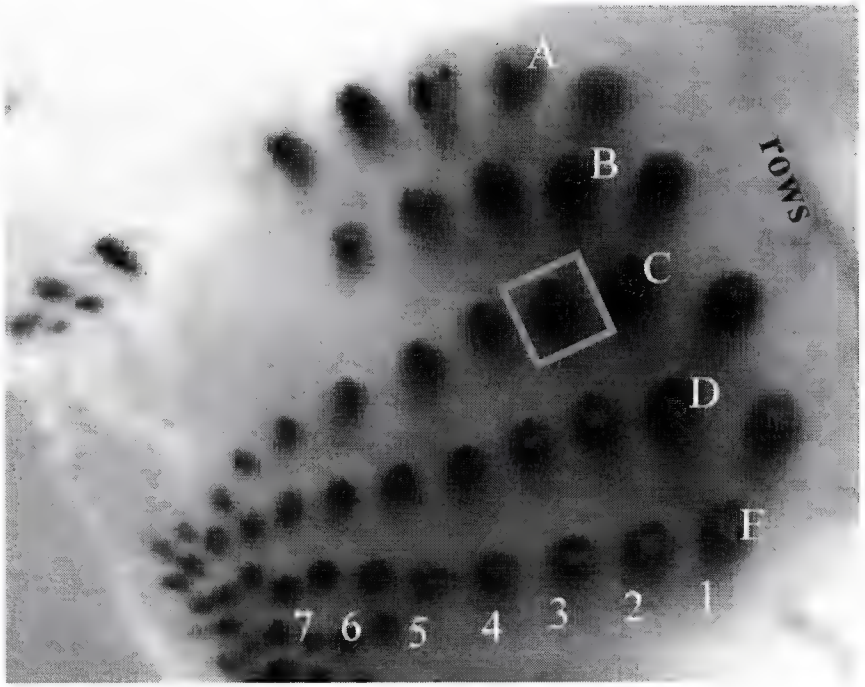


(Knutsen, Pietr, Ahissar, *J Neurosci,* 2006)

Per Knutsen

Effect of spatial configuration

Maciej Pietr

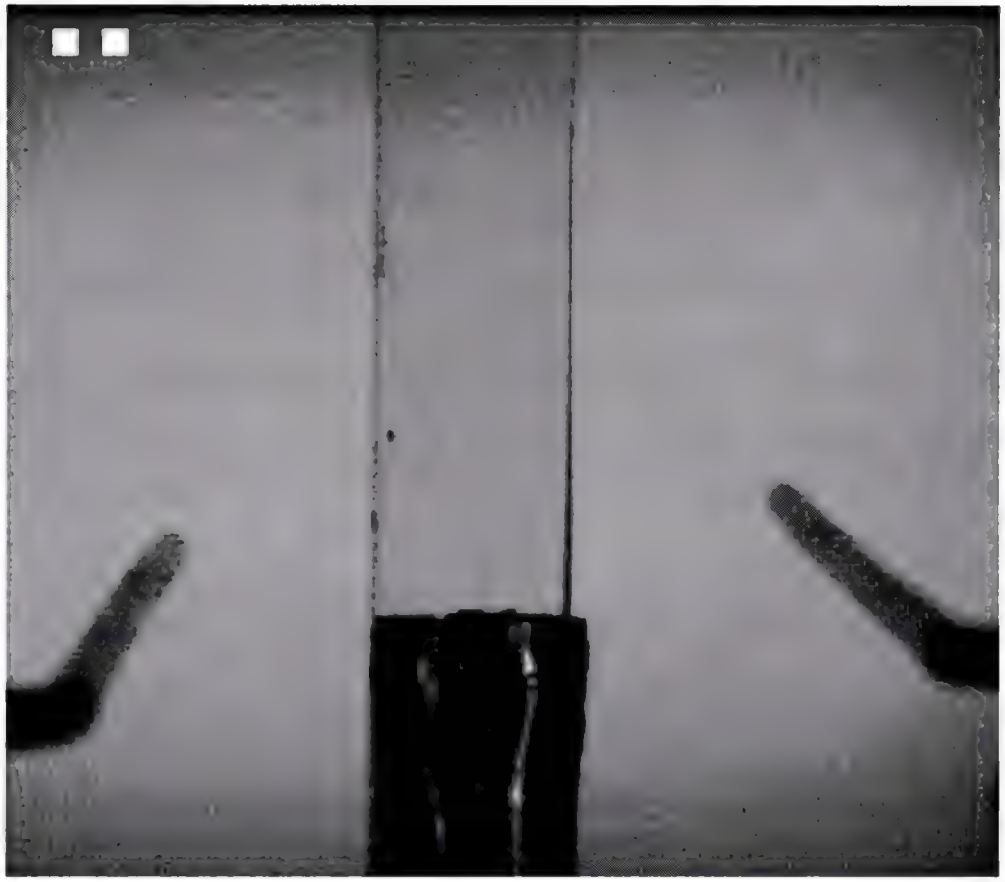


(Knutsen, Pietr, Ahissar, *J Neurosci,* 2006)

Per Knutsen

Effect of spatial configuration

Maciej Pietr



137_271003_1_37_B_50fps (task single whiskers) compressed

(Knutsen, Pietr, Ahissar, *J Neurosci,* 2006)

Possible coding of horizontal location

Spatial code?

Hyperacuity ==> ~~Identity code?~~ ~~(labeled line)~~

Single whisker localization ==> ~~Interpolation code?~~

Rate code?

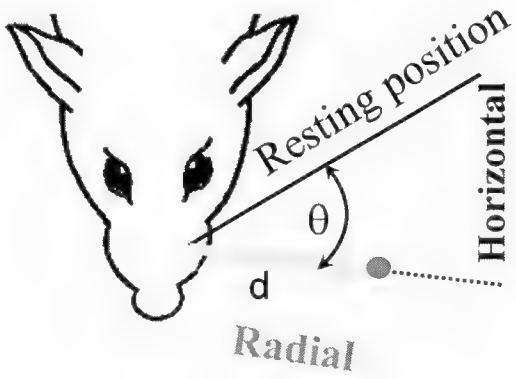
Temporal code?

proprioceptive?

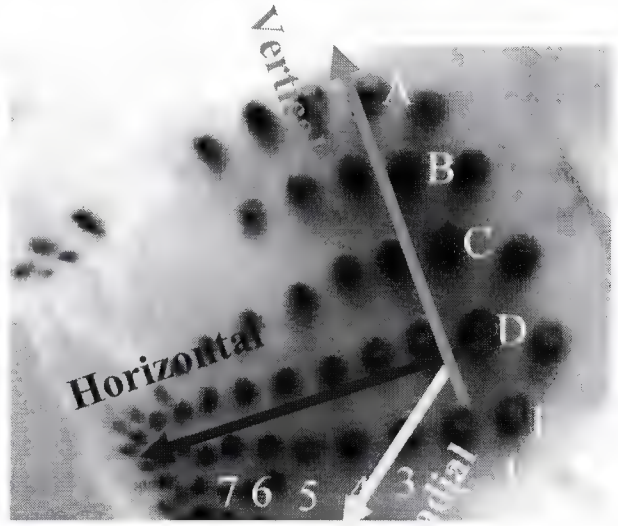
Coordinates of object location

Radial

Whisker-centered



Head-centered



Krupa, Matell, Brisben, Oliveira, Nicolelis, *J Neurosci*, 2001

Radial localization

- does not require whisker movements
- improves with the number of intact whiskers
- But does not depend on their identity

Krupa, Matell, Brisben, Oliveira, Nicolelis, *J Neurosci*, 2001

Possible coding of radial location

Spatial code?

~~Identity code?~~ (labeled line)

~~Interpolation code?~~

Rate code?

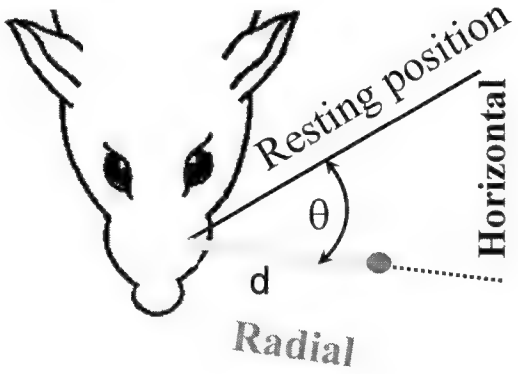
Temporal code?

proprioceptive?

Krupa, Matell, Brisben, Oliveira, Nicolelis, *J Neurosci*, 2001

From behavior

Whisker-centered



~~Spatial labeled-line code?~~

~~Spatial interpolation code?~~

Rate code?

Temporal code?

proprioceptive?

~~Spatial labeled-line code?~~

Spatial interpolation code?

Rate code?

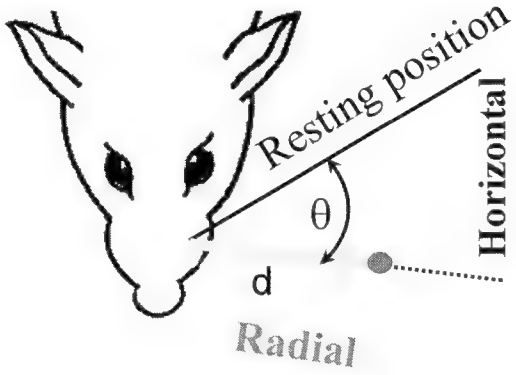
~~Temporal code?~~

proprioceptive?

(Knutsen & Ahissar, *TINS,* 2009)

From behavior

Whisker-centered



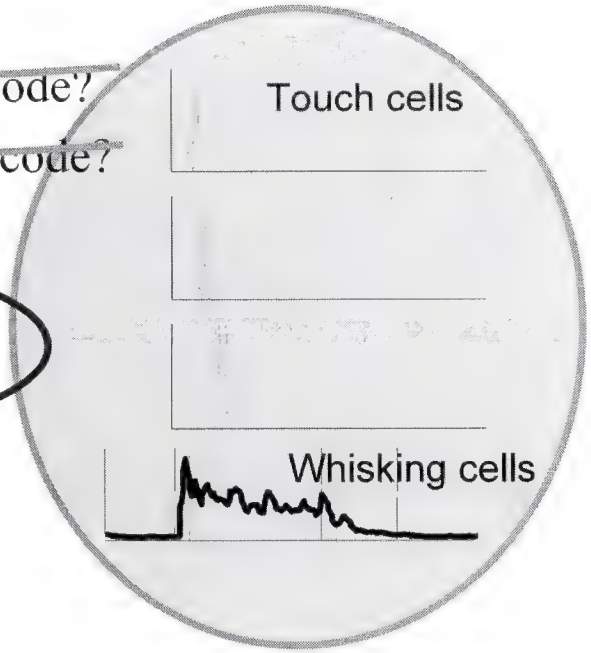
~~Spatial labeled-line code?~~

~~Spatial interpolation code?~~

~~Rate code?~~

Temporal code

proprioceptive



~~Spatial labeled-line code?~~

Spatial interpolation code

Rate code'

~~Temporal code?~~

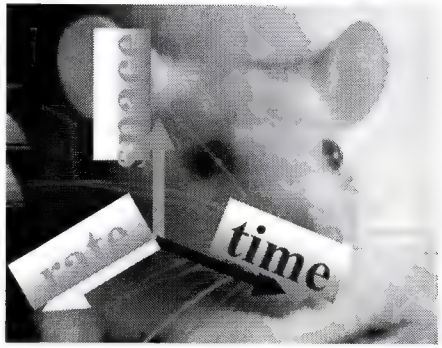
~~proprioceptive?~~

From neuronal recordings

(Knutsen & Ahissar, *TINS,* 2009)

Orthogonal coding

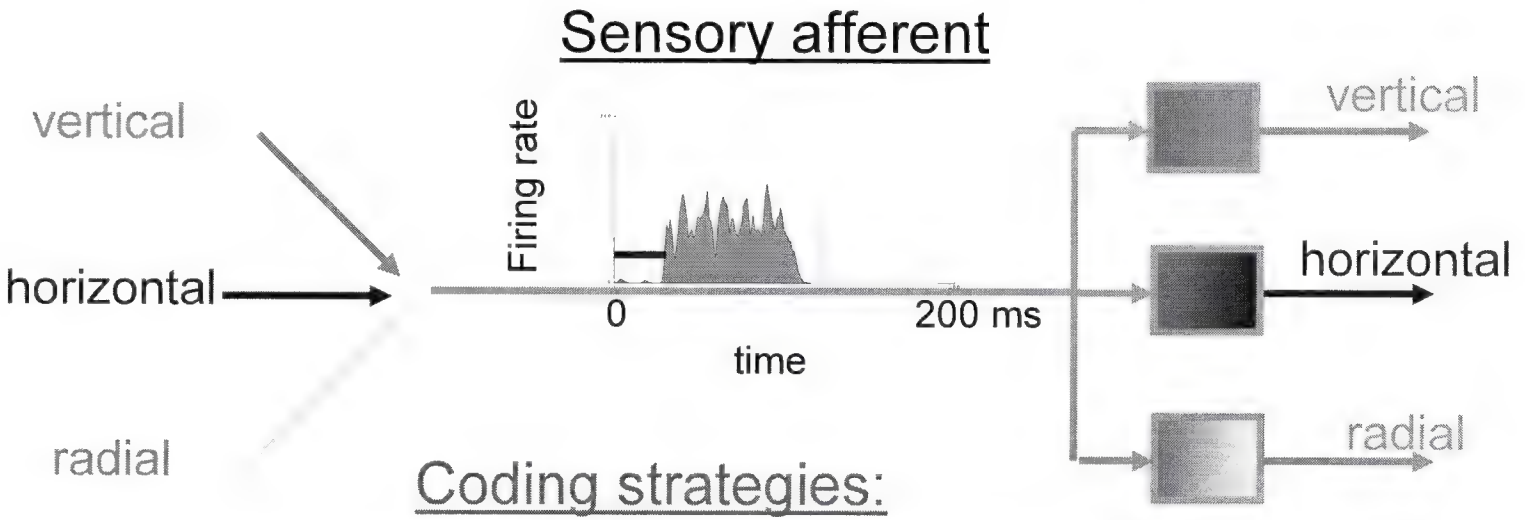
(Knutsen & Ahissar, *TINS,* 2009)



Orthogonal location coding

object

brain



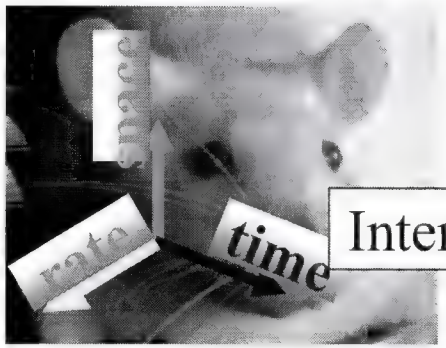
Coding strategies:

Different variables same neurons
vs
Same variable different neurons

(Knutsen & Ahissar, *TINS,* 2009)

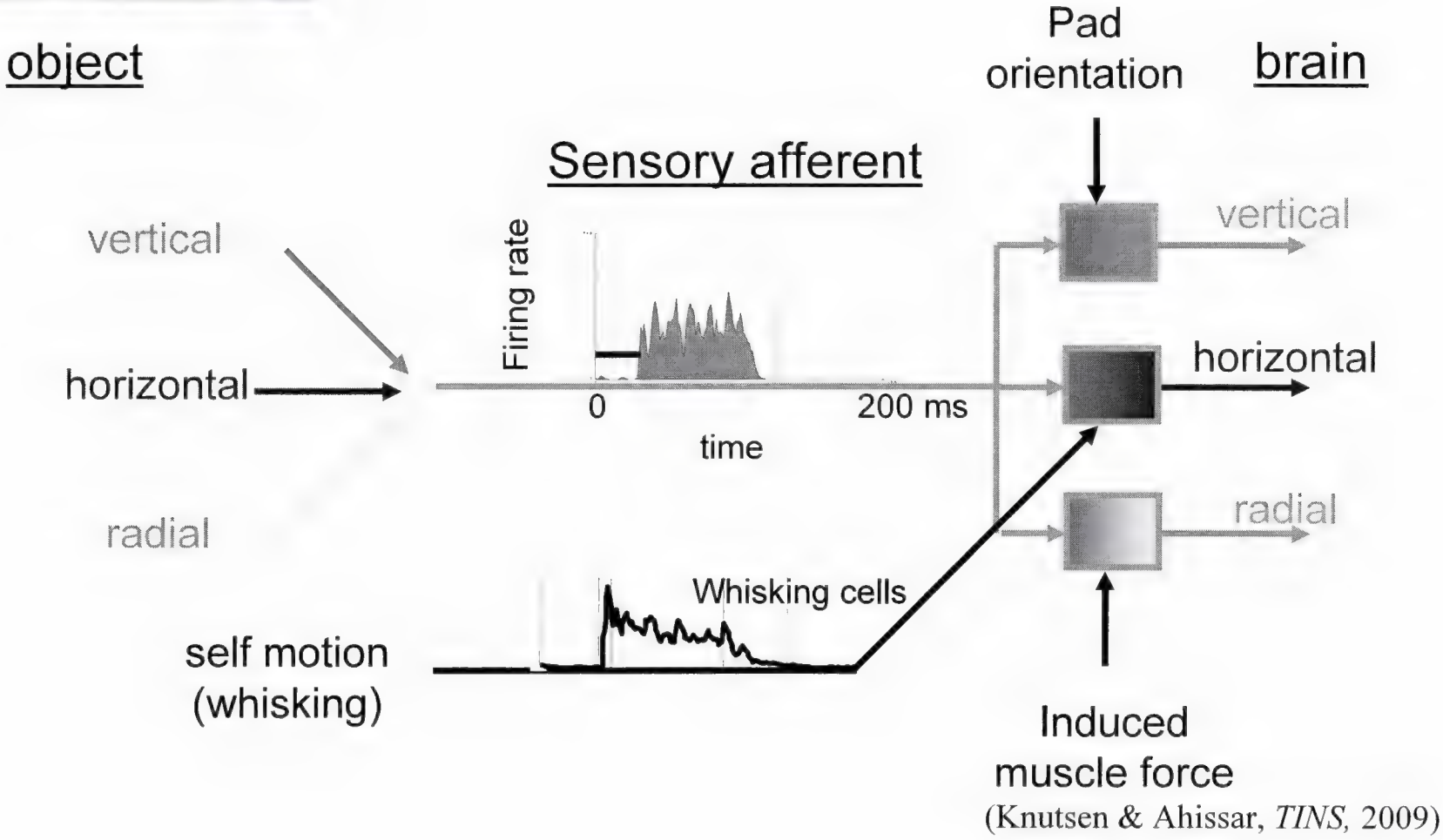
Dependency on self motion

(Knutsen & Ahissar, *TINS,* 2009)



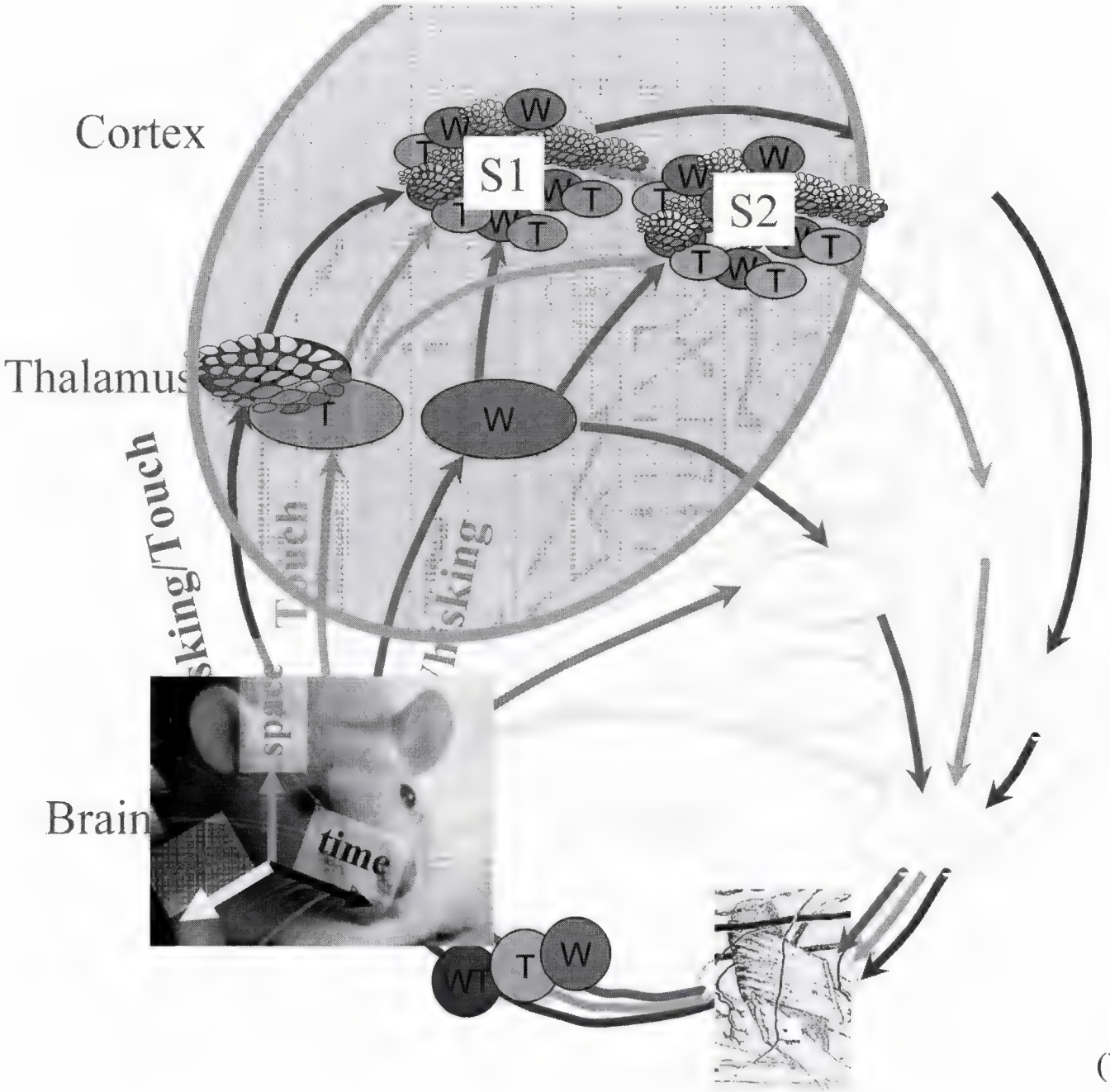
Object location coding

Internal representations depend on self-motion



(Knutsen & Ahissar, *TINS,* 2009)

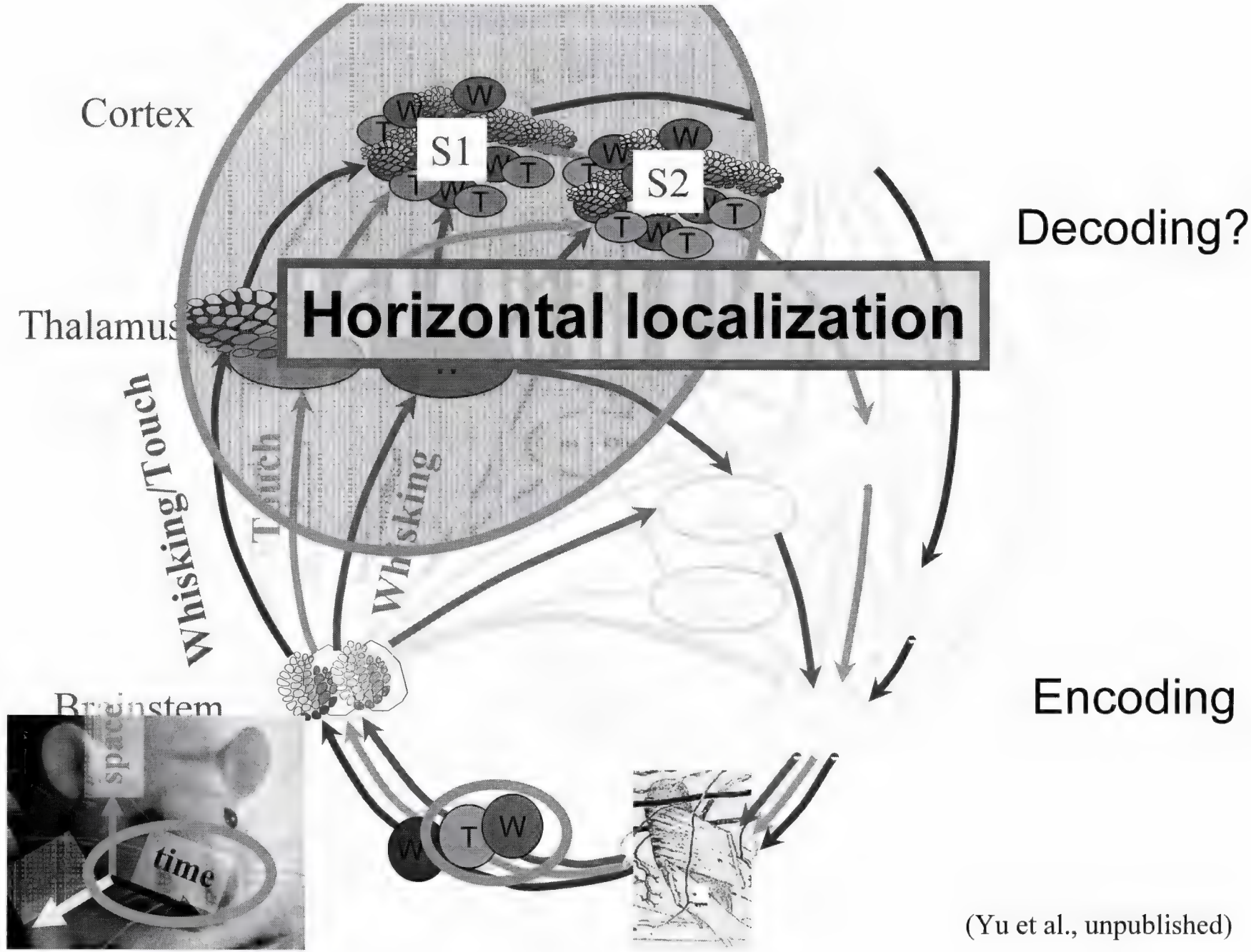
Decoding



Decoding?

Encoding

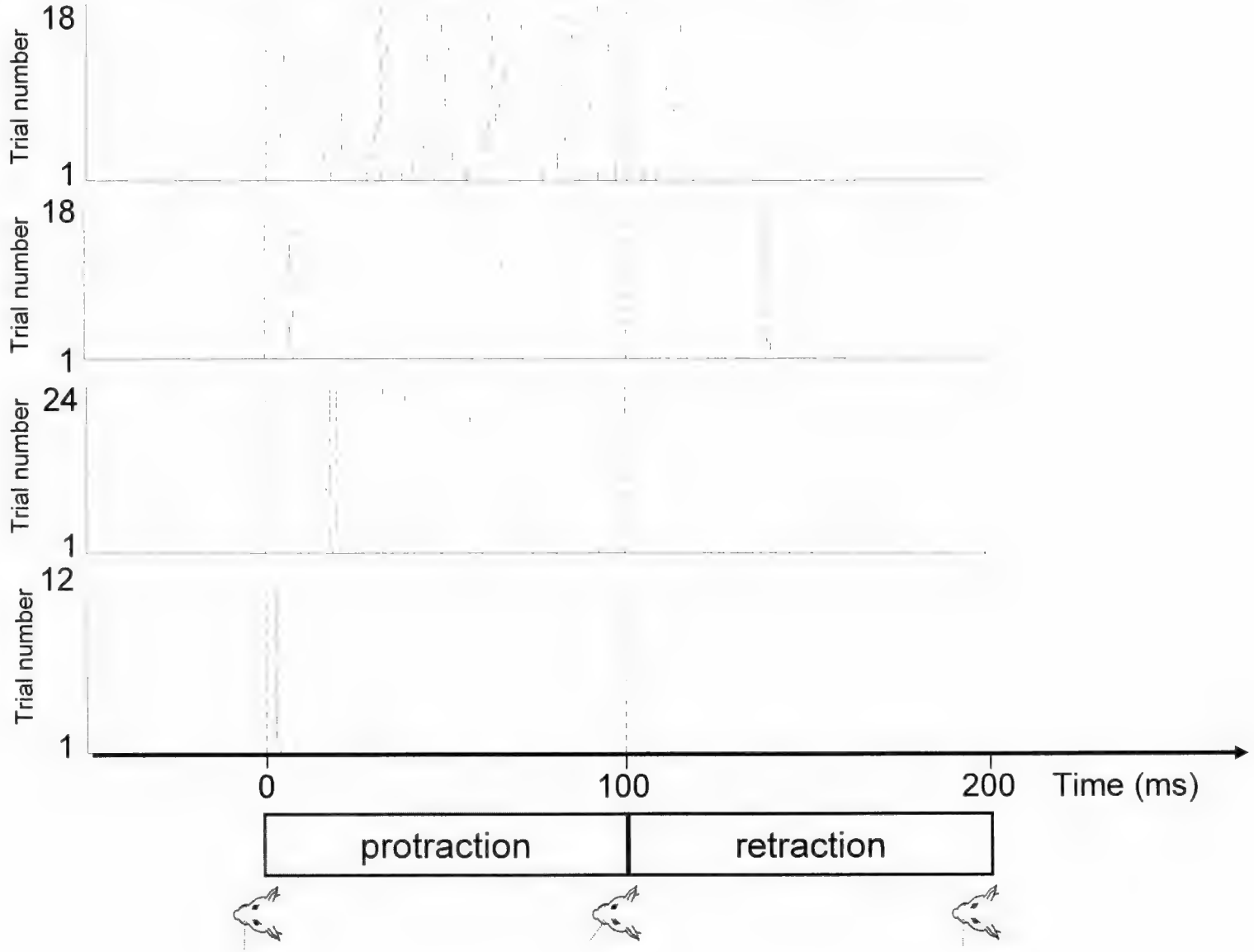
(Yu et al., unpublished)



(Yu et al., unpublished)

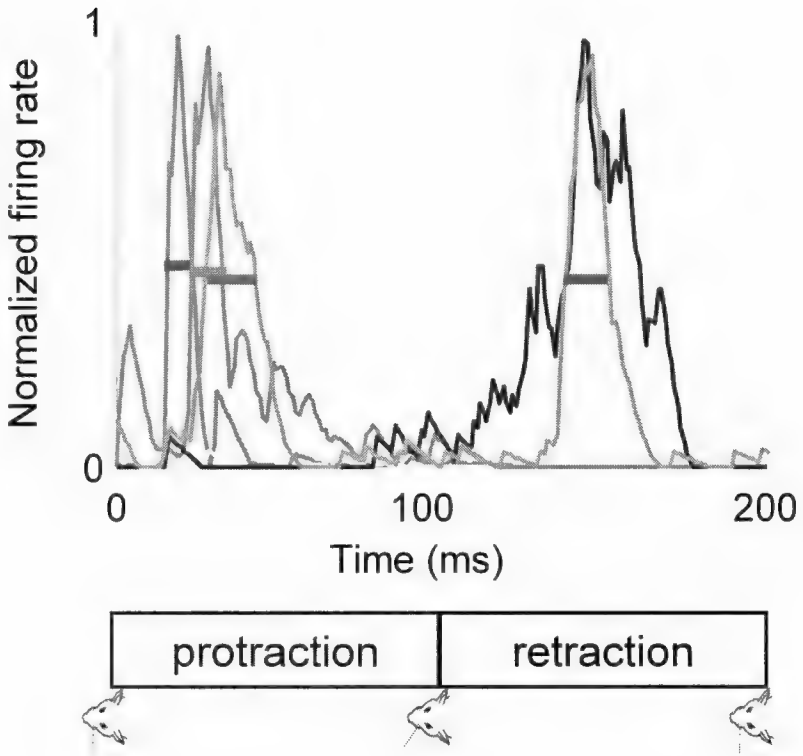
Need position and contact signals

Phase coding of single Whisking cells

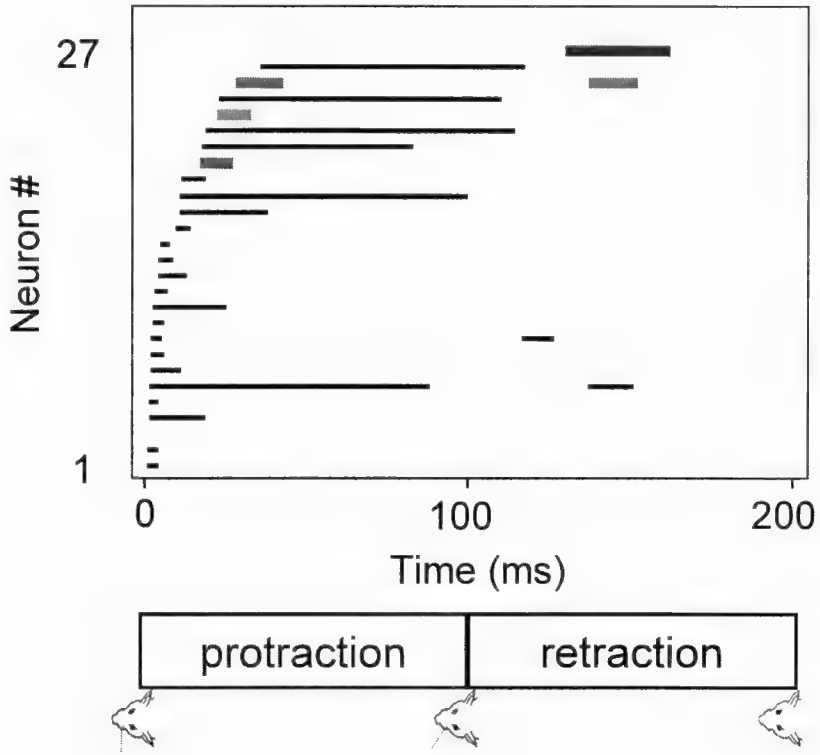


Phase coding of Whisking cells

PSTH



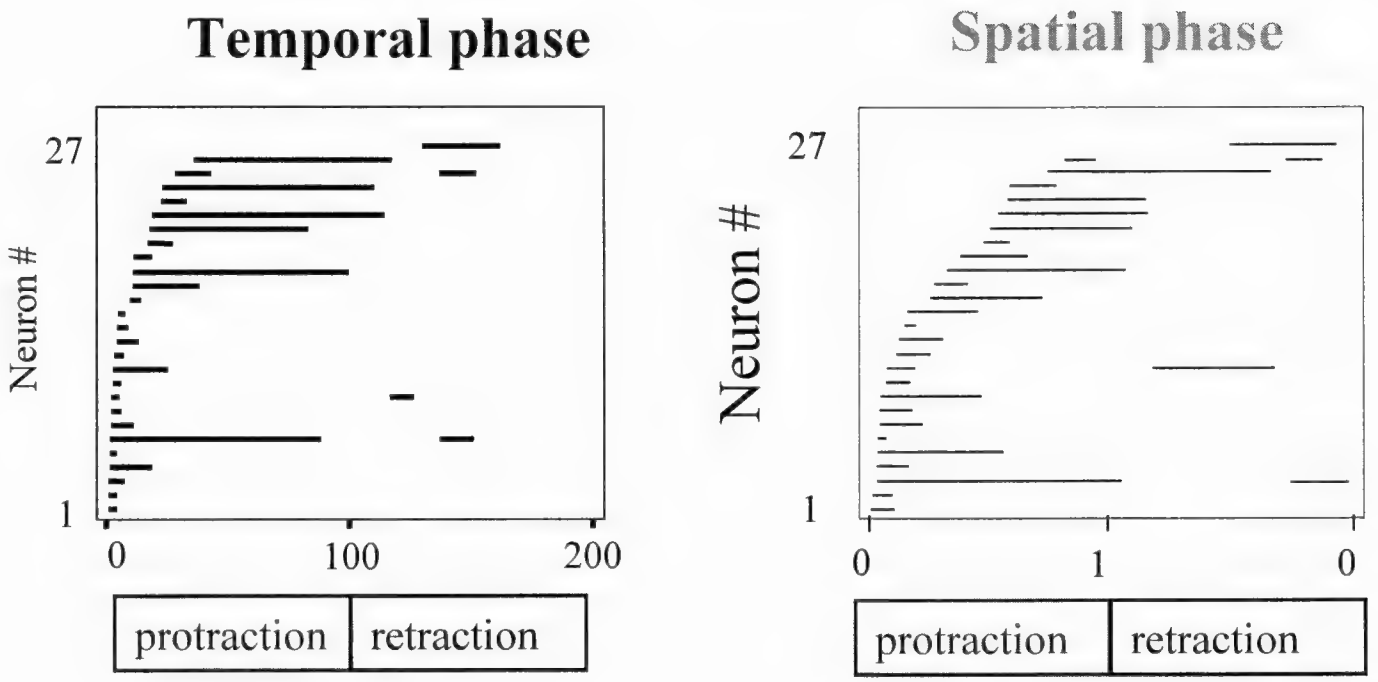
Firing fields



Phase coding of Whisking cells

(All Whisking and Whisking/Touch cells)

Phase fields

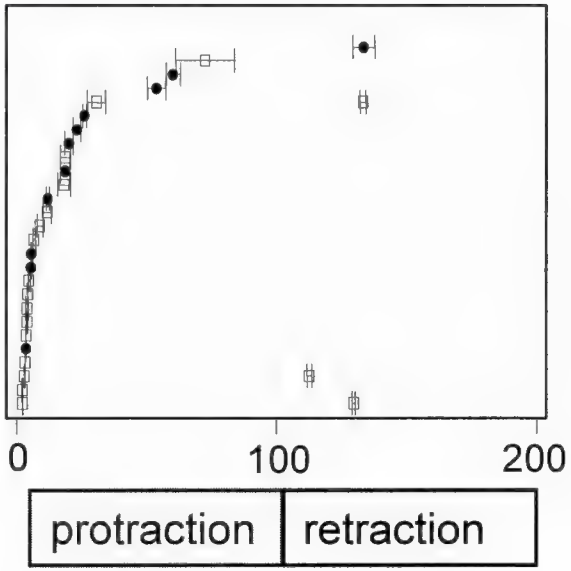


Time from protraction onset (ms)

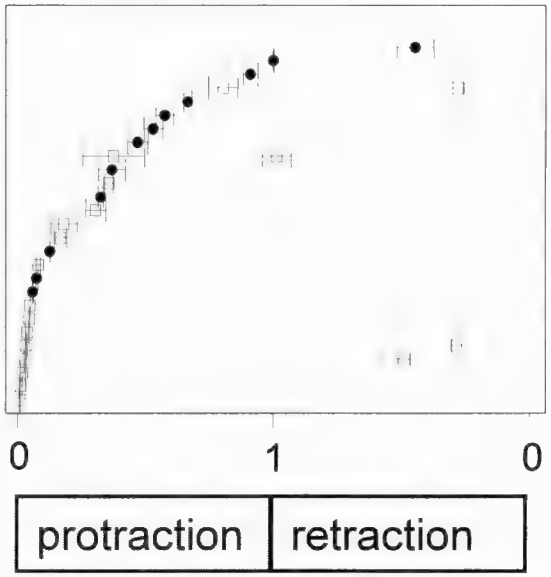
Phase coding of Whisking cells

Phase onsets

Temporal Phase



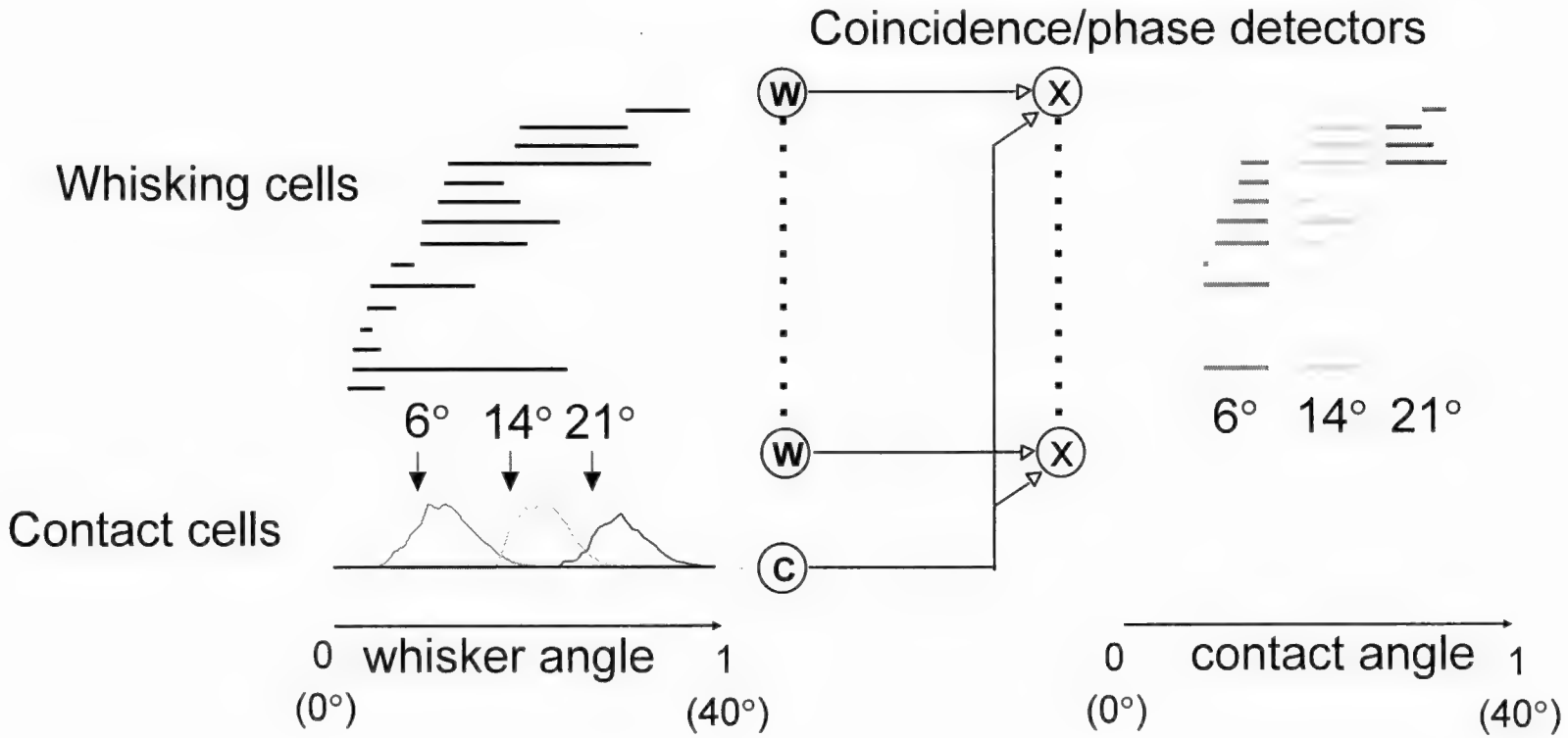
Spatial phase



Whisking phase

Encoding-decoding schemes

Spatio-temporal scheme

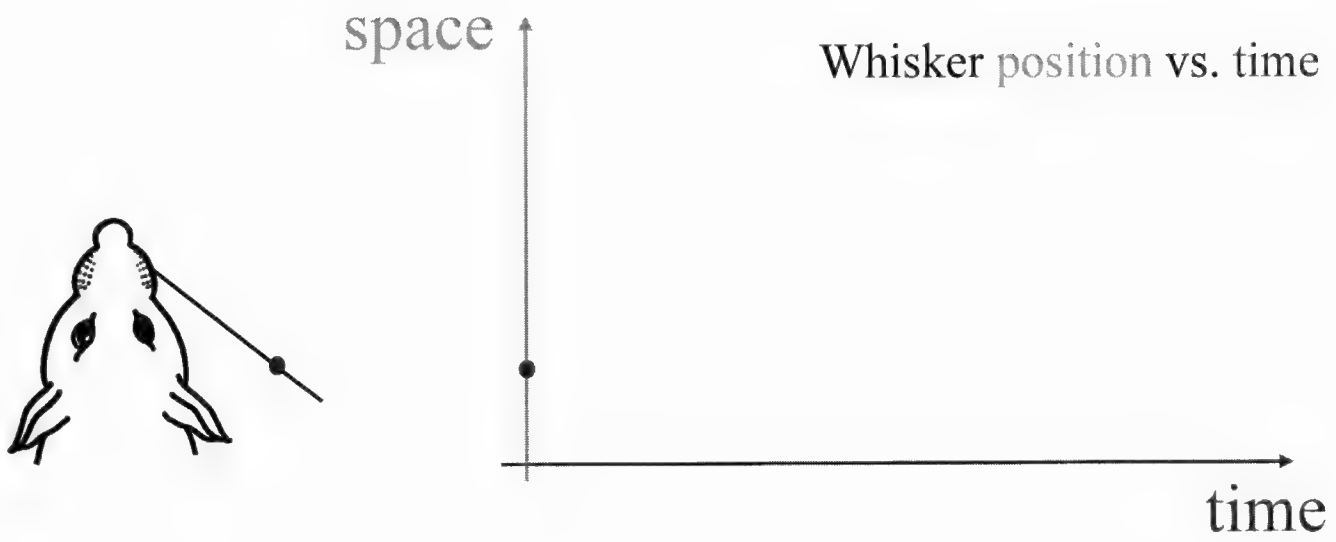


What the whiskers tell the rat brain

Whisking

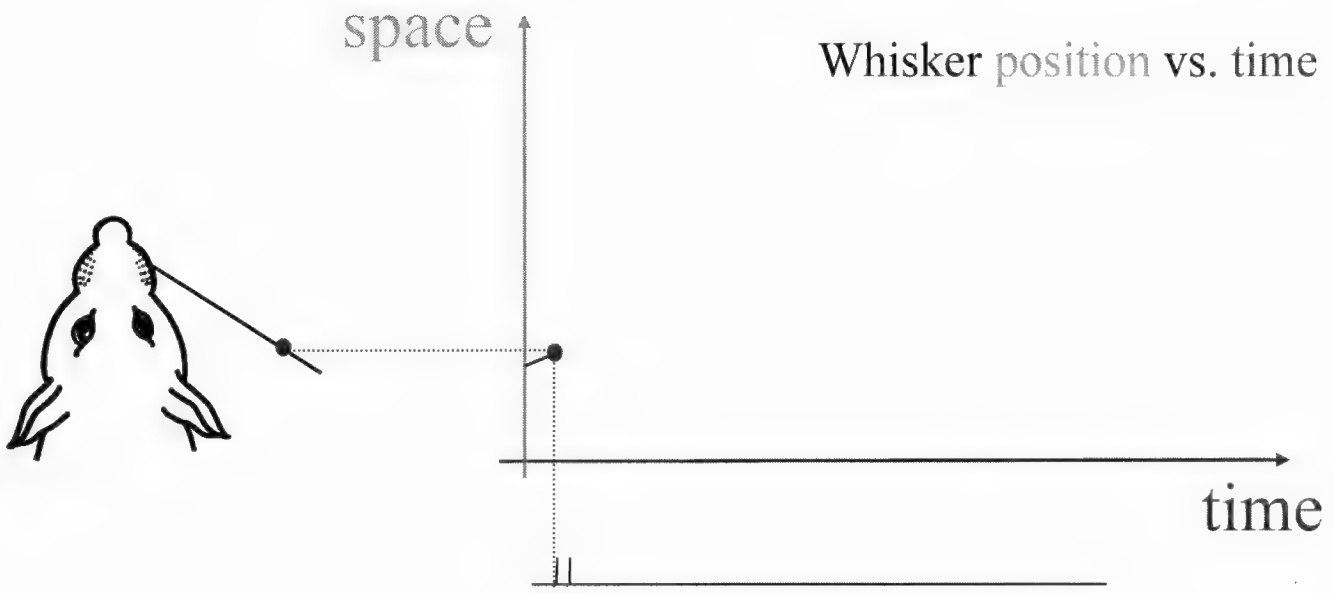
What the whiskers tell the rat brain

Whisking



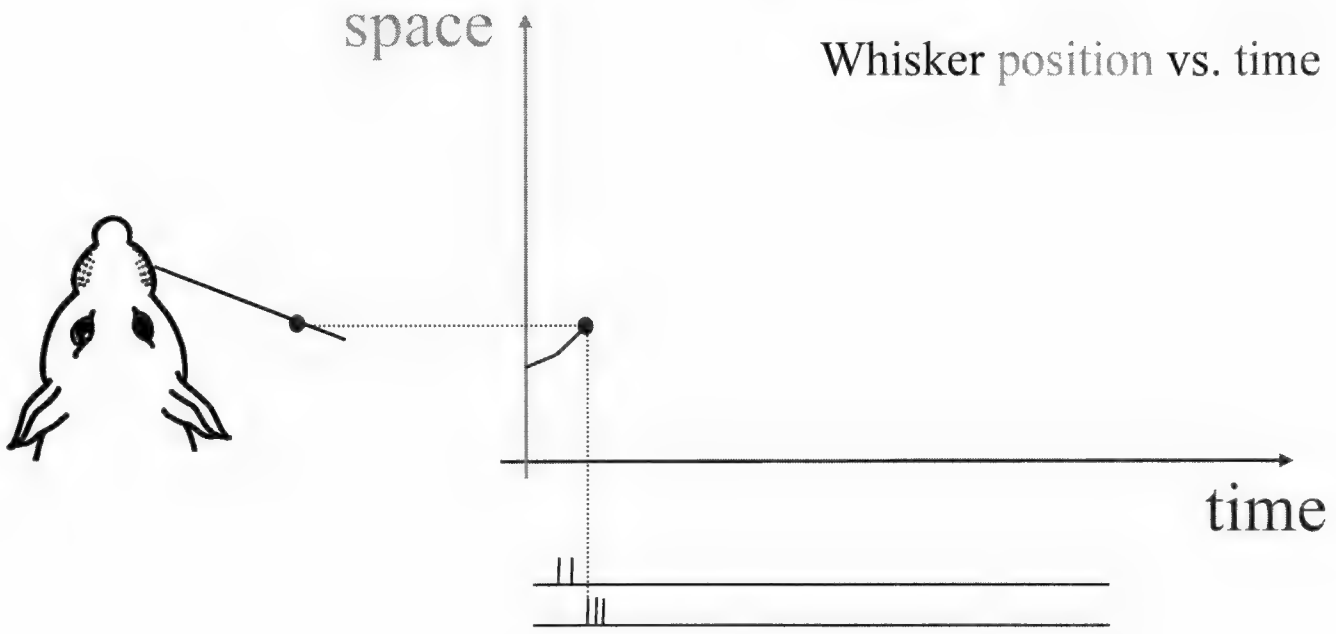
What the whiskers tell the rat brain

Whisking



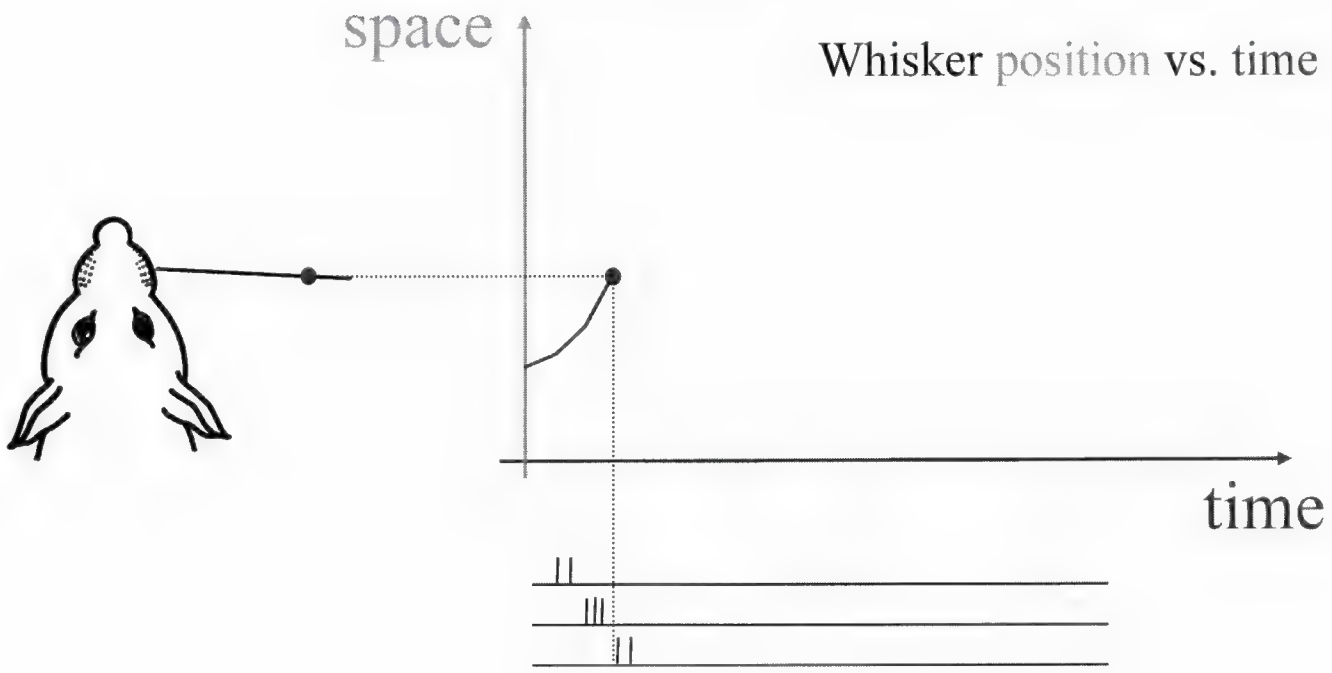
What the whiskers tell the rat brain

Whisking



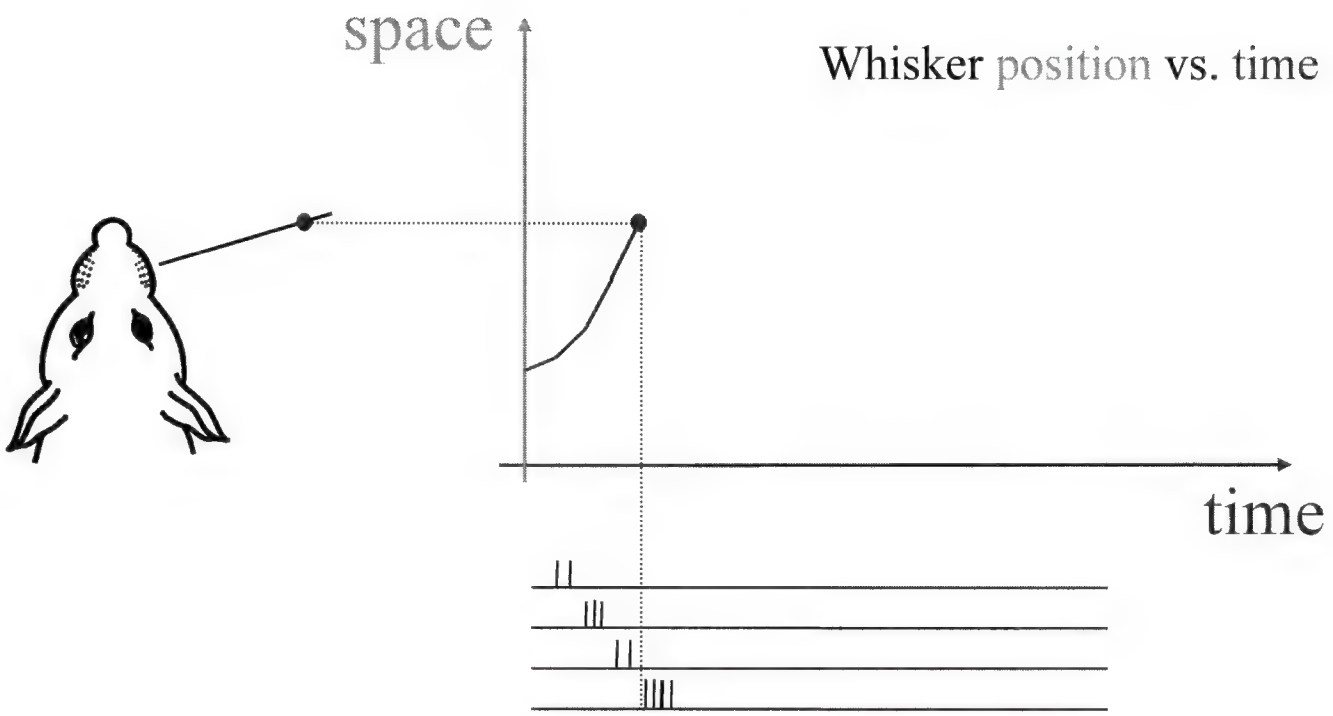
What the whiskers tell the rat brain

Whisking



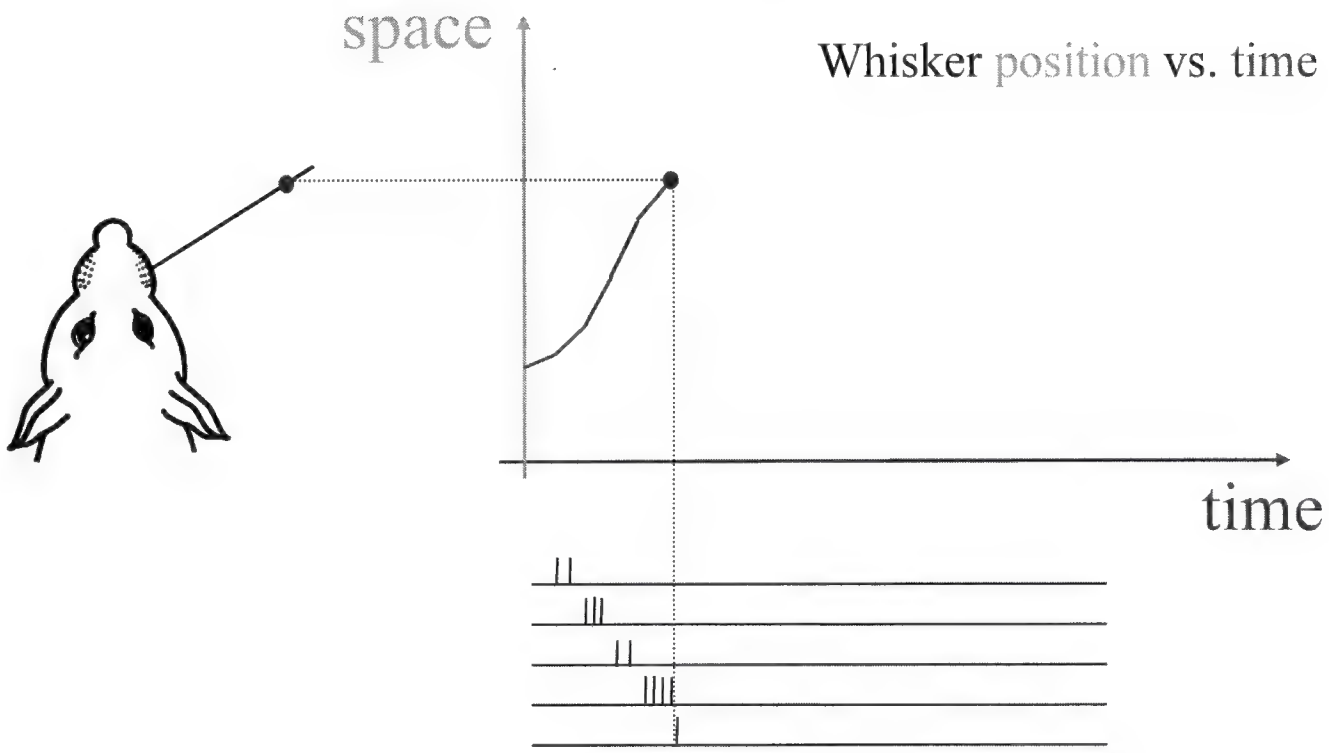
What the whiskers tell the rat brain

Whisking



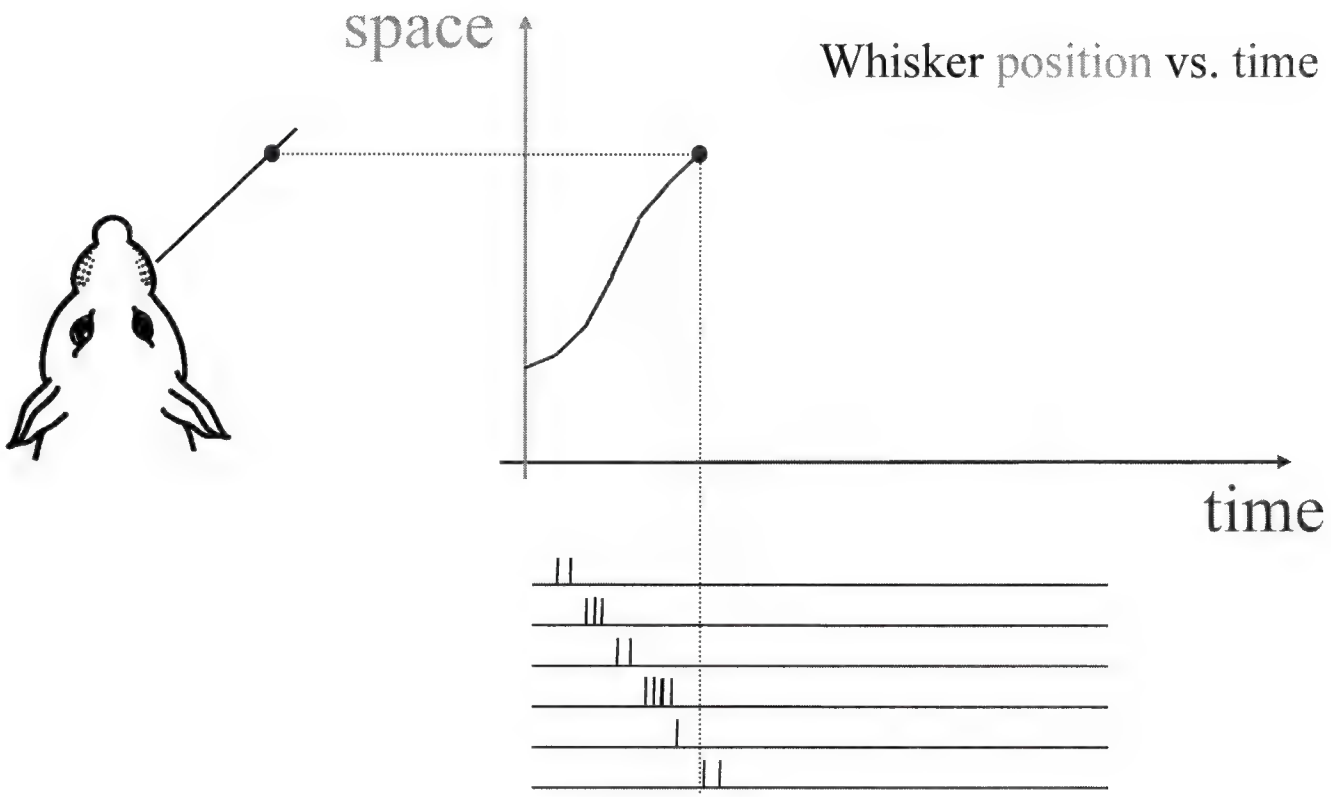
What the whiskers tell the rat brain

Whisking



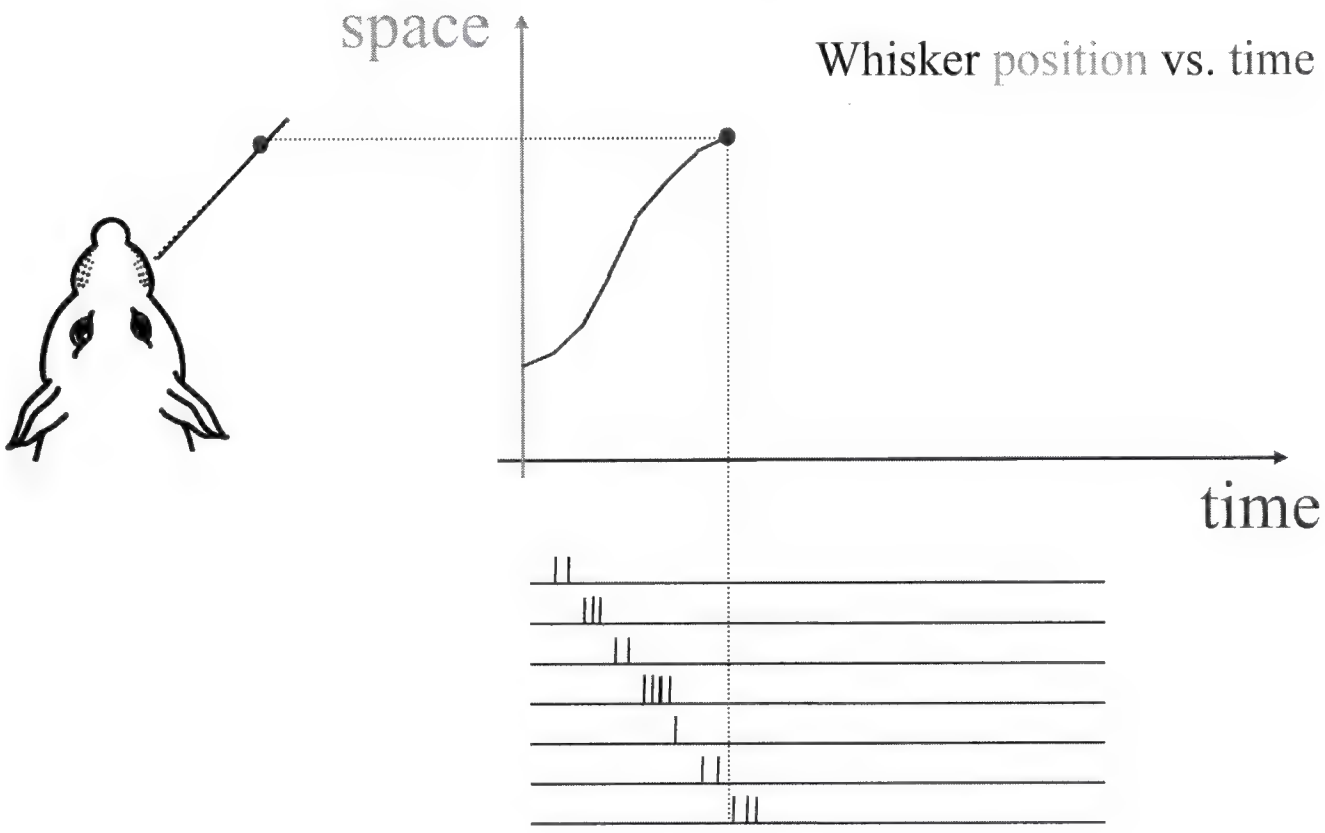
What the whiskers tell the rat brain

Whisking



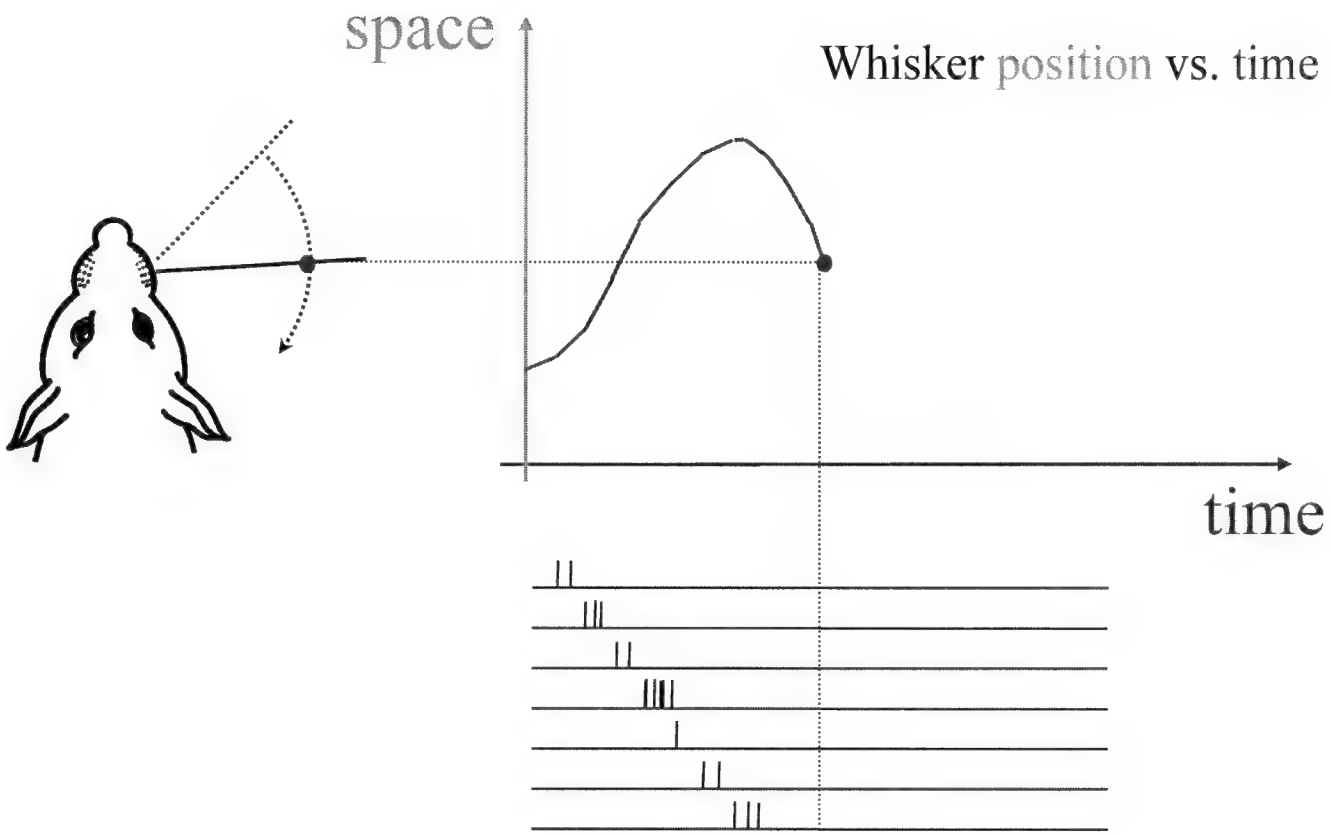
What the whiskers tell the rat brain

Whisking



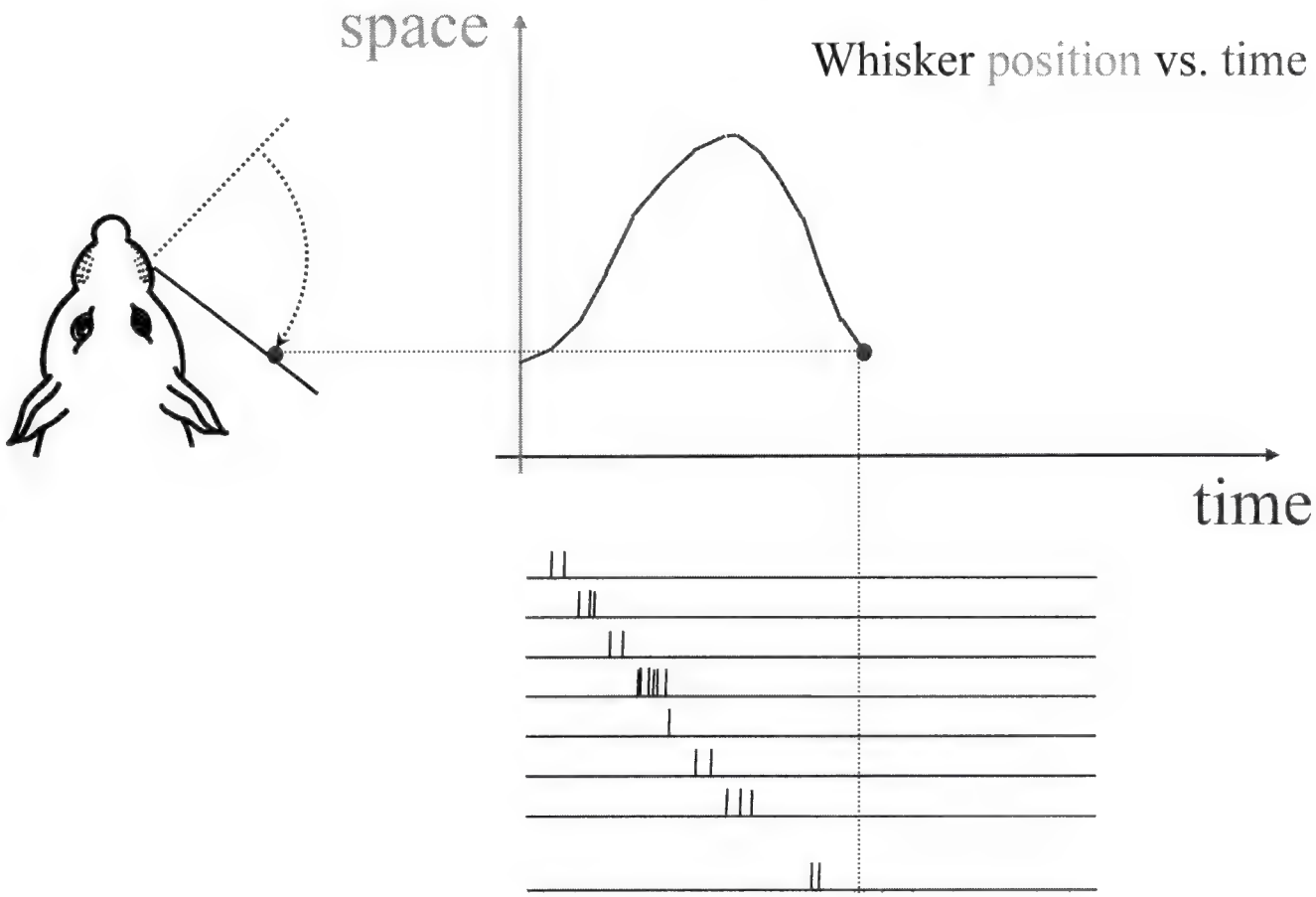
What the whiskers tell the rat brain

Whisking



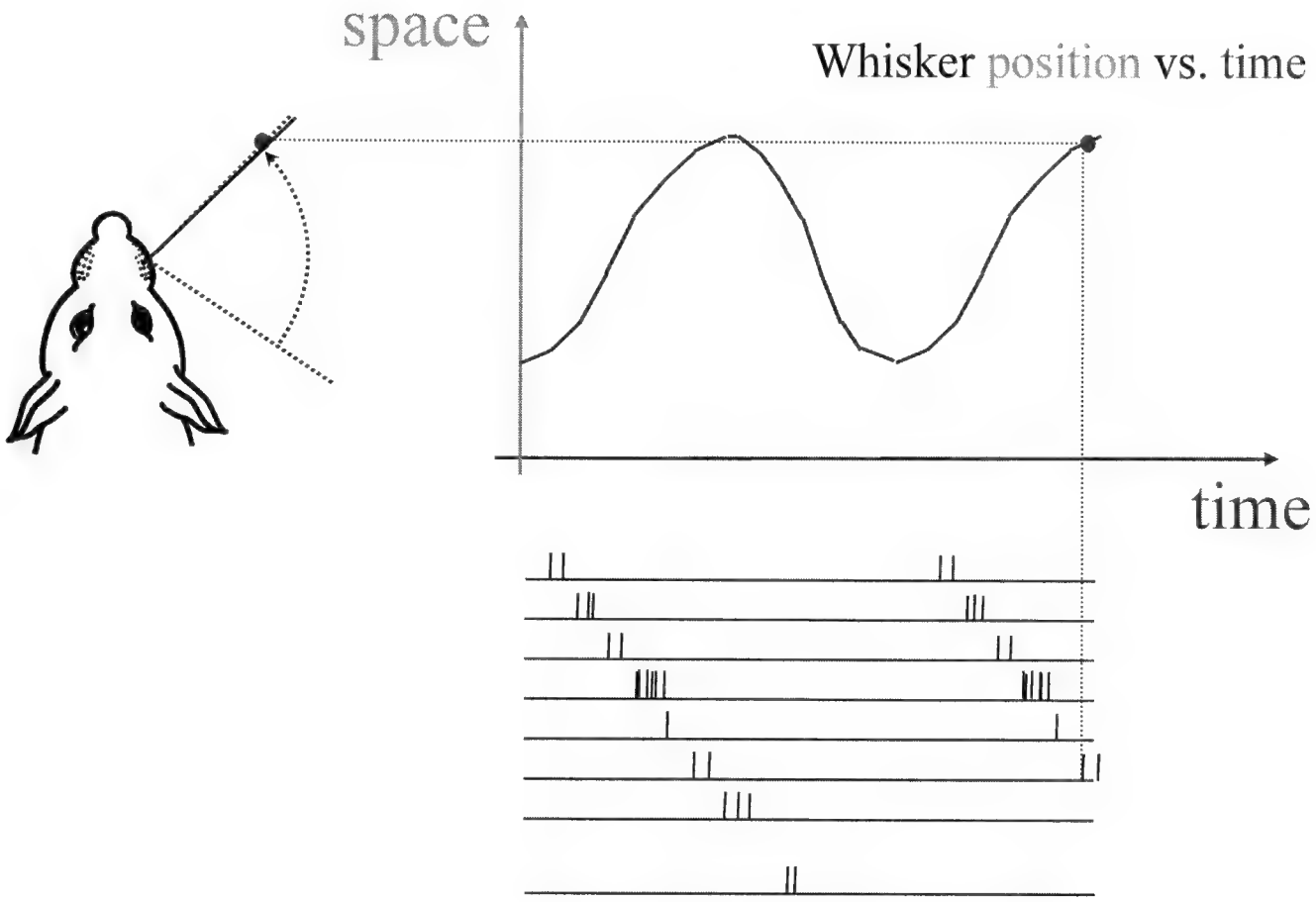
What the whiskers tell the rat brain

Whisking



What the whiskers tell the rat brain

Whisking

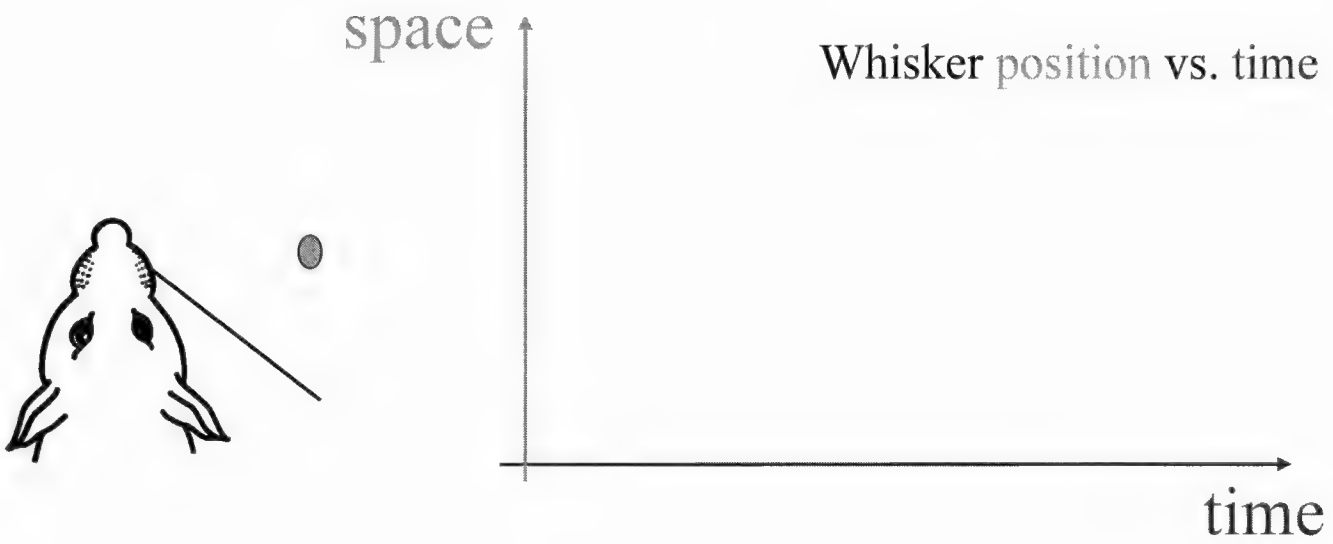


What the whiskers tell the rat brain

Touch

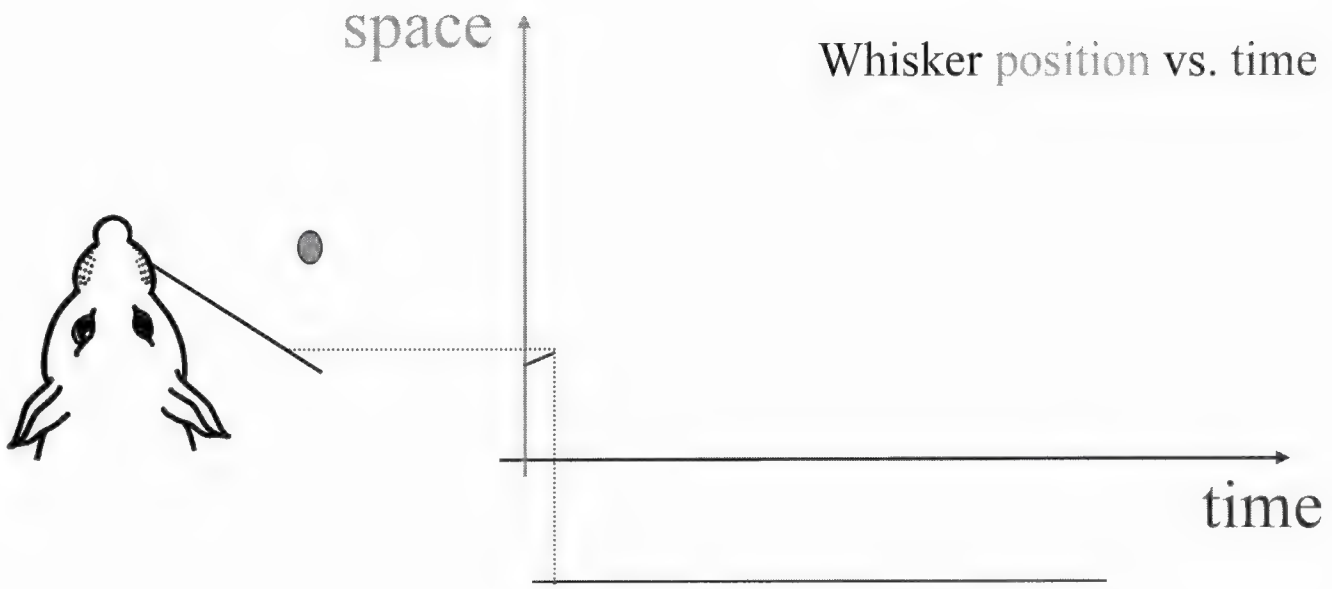
What the whiskers tell the rat brain

Touch



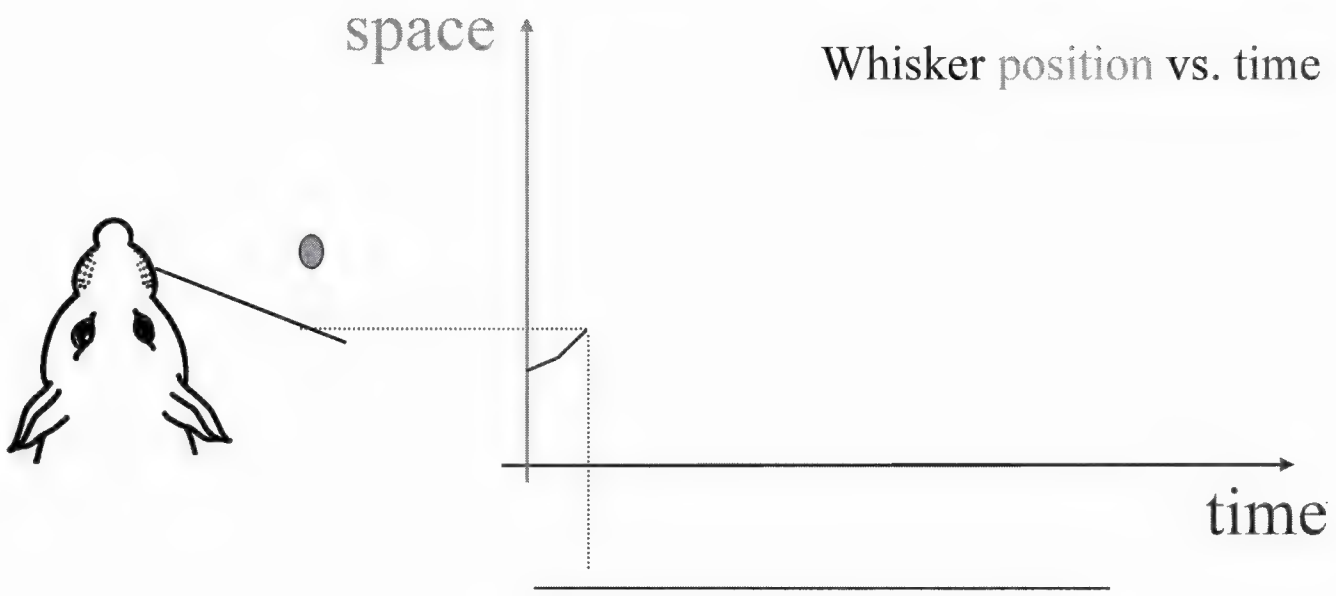
What the whiskers tell the rat brain

Touch



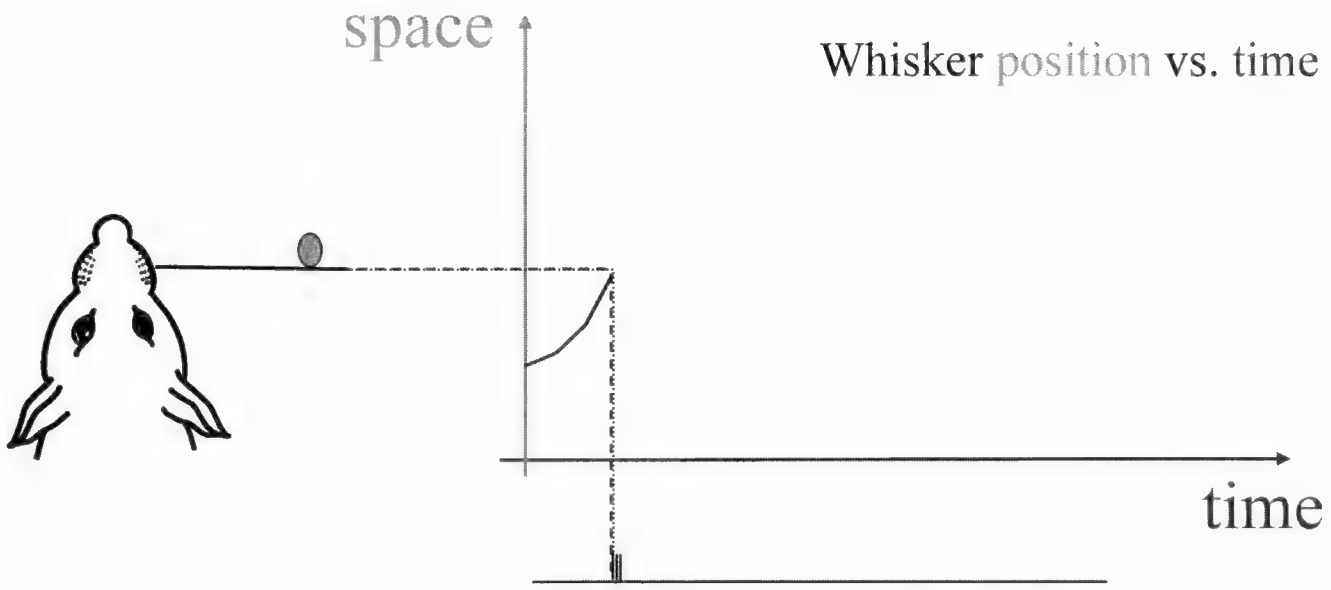
What the whiskers tell the rat brain

Touch



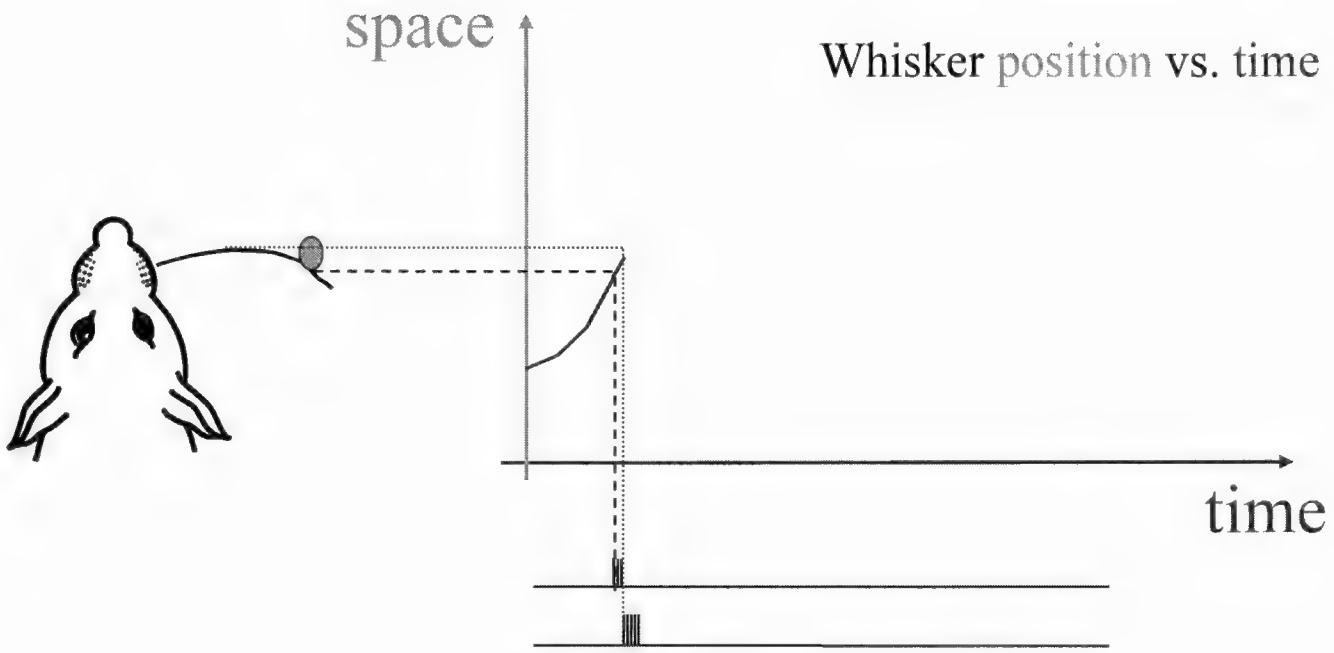
What the whiskers tell the rat brain

Touch



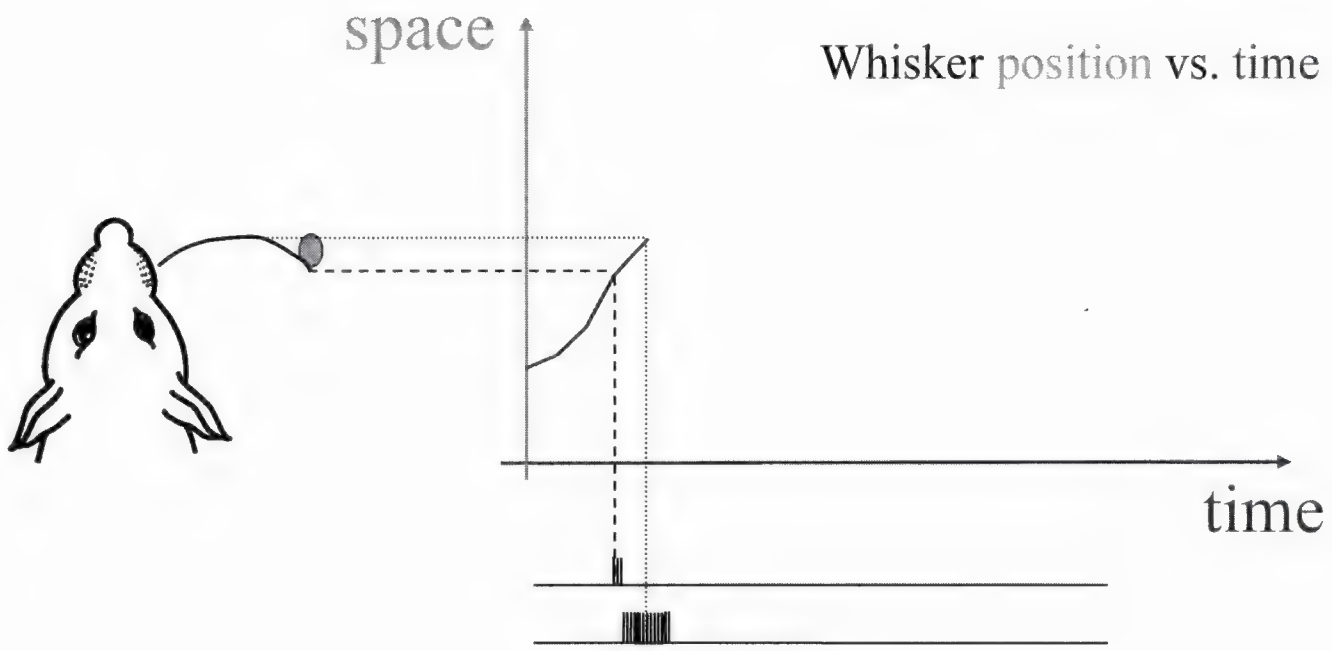
What the whiskers tell the rat brain

Touch



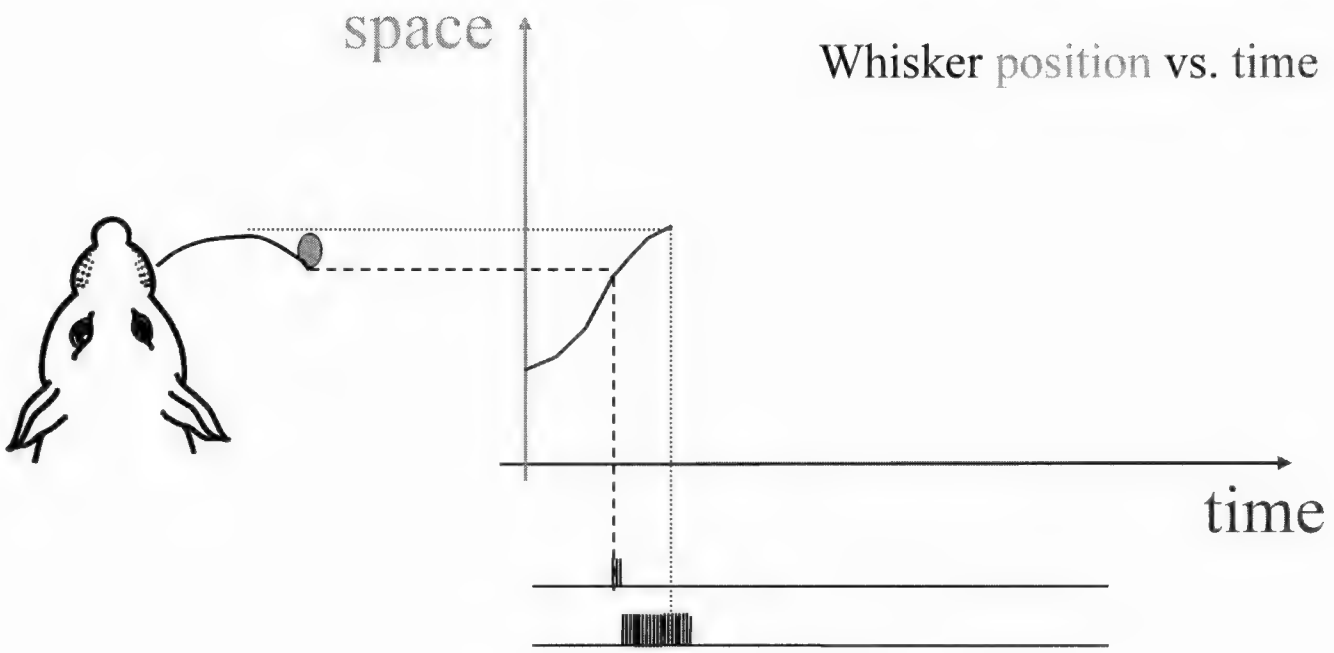
What the whiskers tell the rat brain

Touch



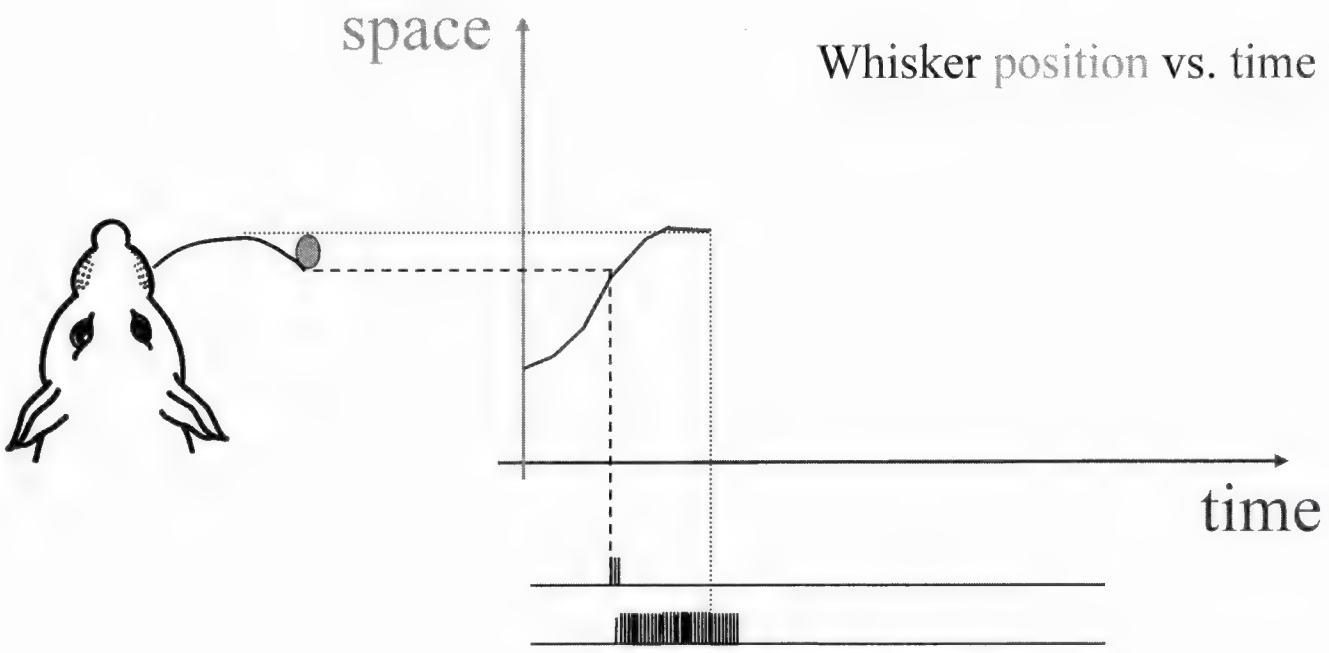
What the whiskers tell the rat brain

Touch



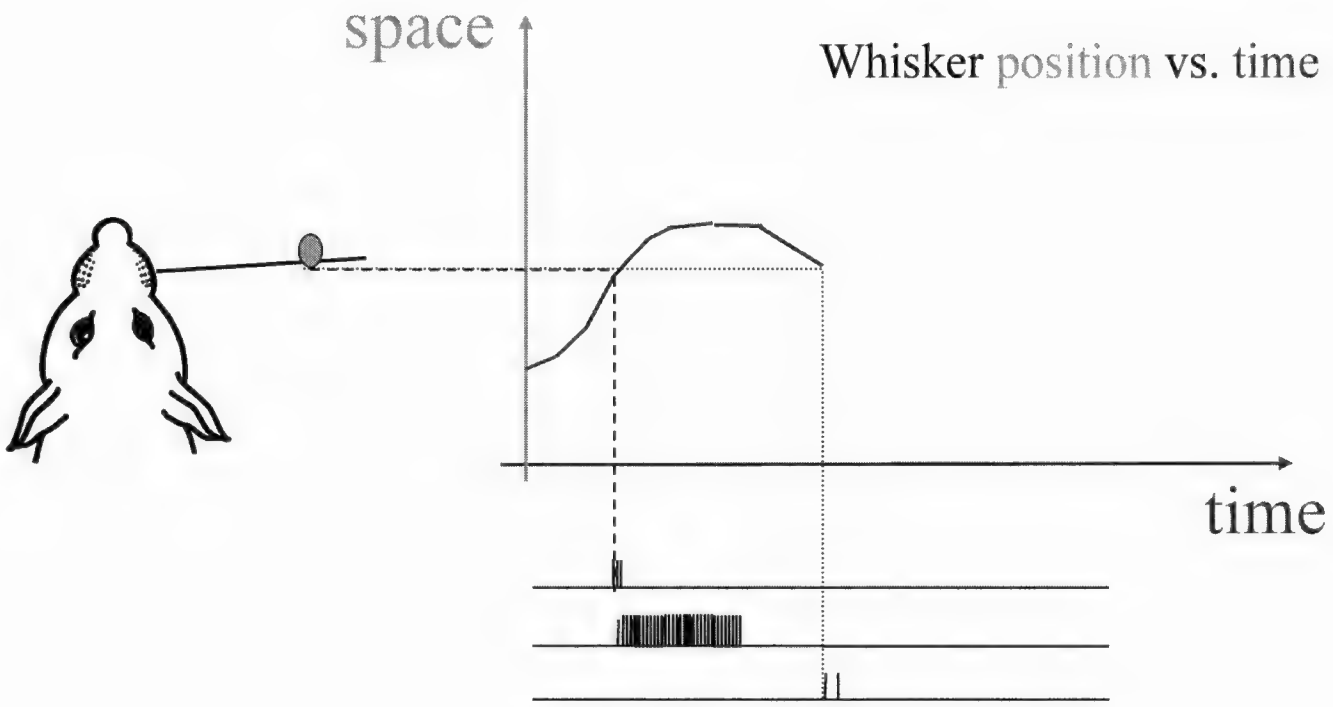
What the whiskers tell the rat brain

Touch



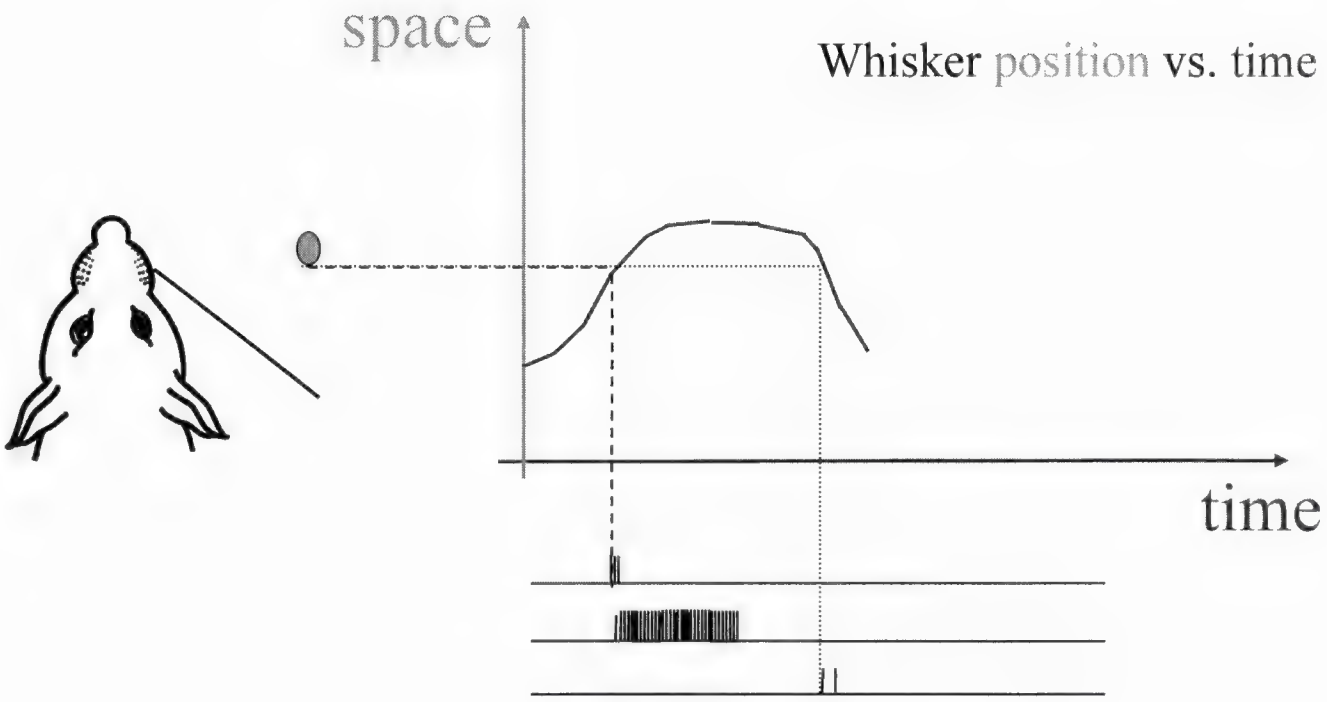
What the whiskers tell the rat brain

Touch



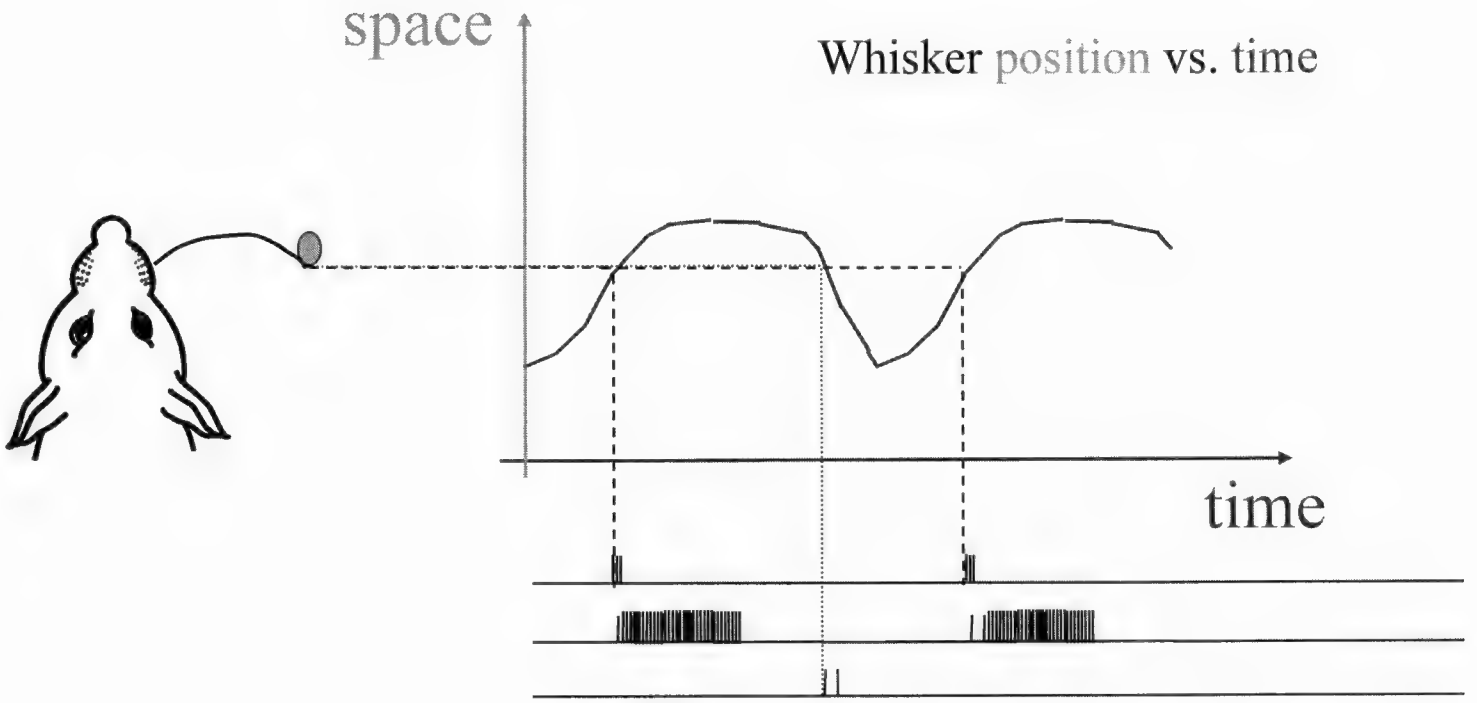
What the whiskers tell the rat brain

Touch



What the whiskers tell the rat brain

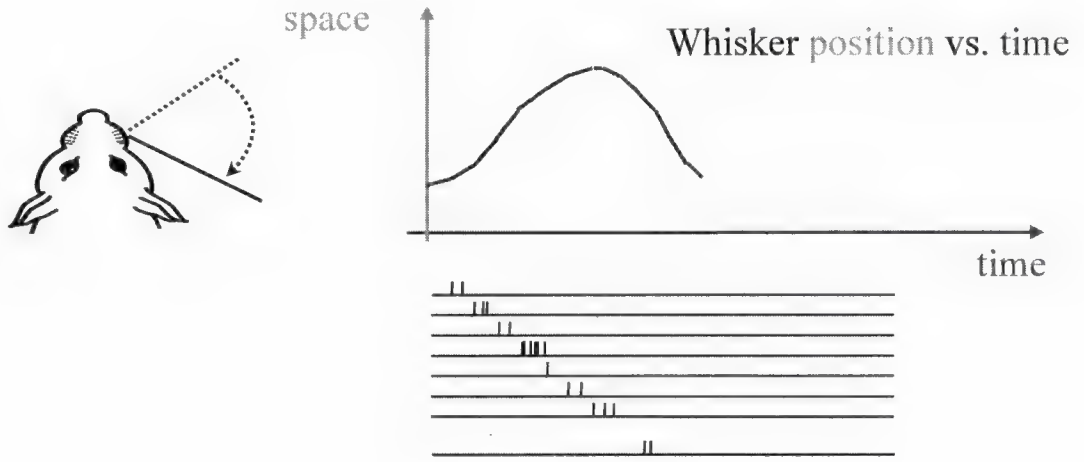
Touch



What the whiskers tell the rat brain

How can the brain use this information?

- Whisking:

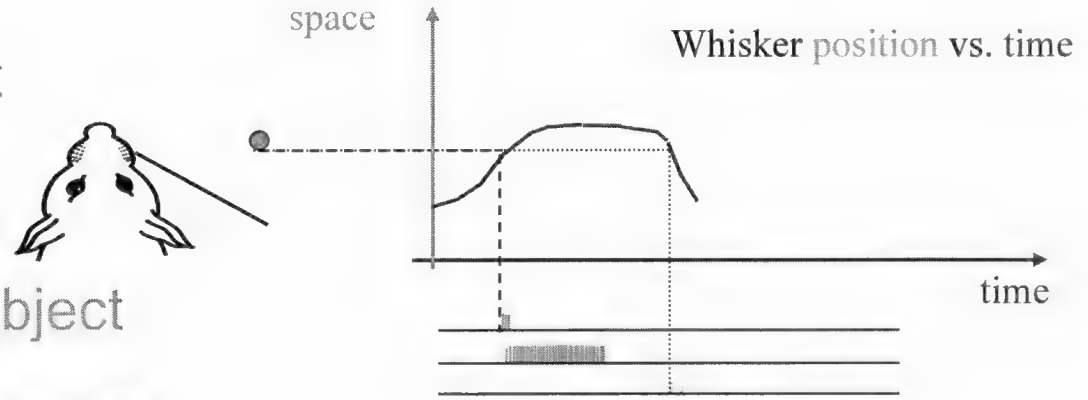


- Touch:

contact with object

pressure against object

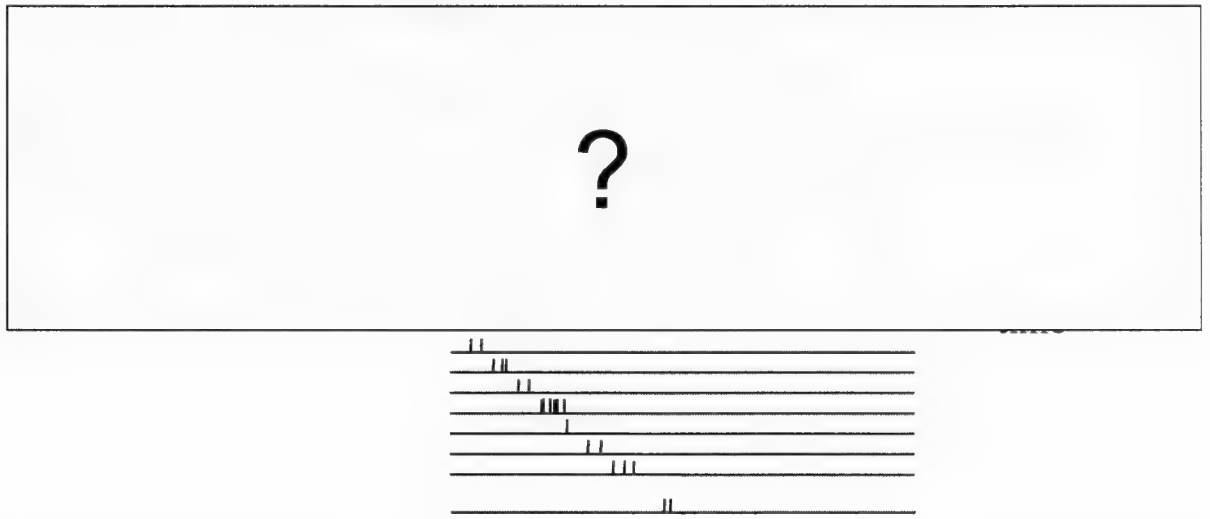
detachment from object



What the whiskers tell the rat brain

How can the brain use this information?

- Whisking:

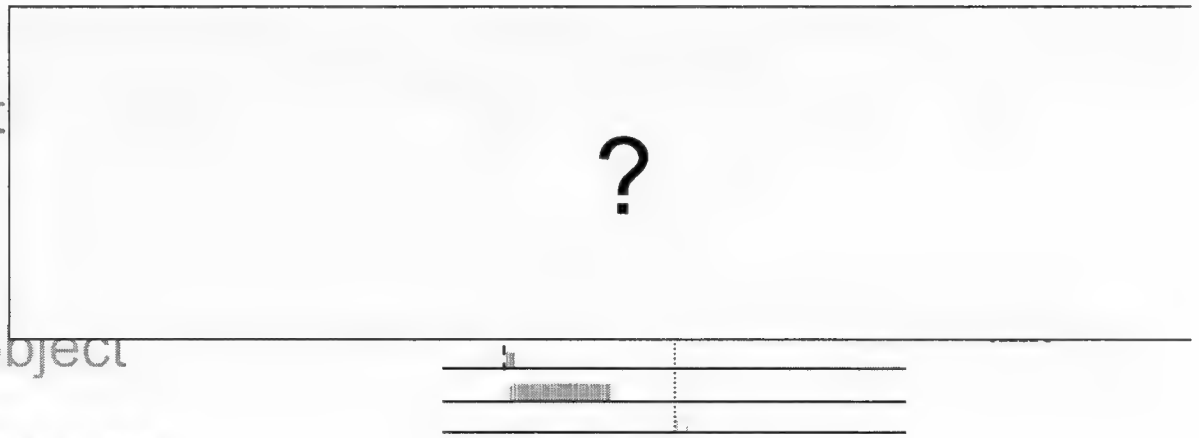


- Touch:

contact with object

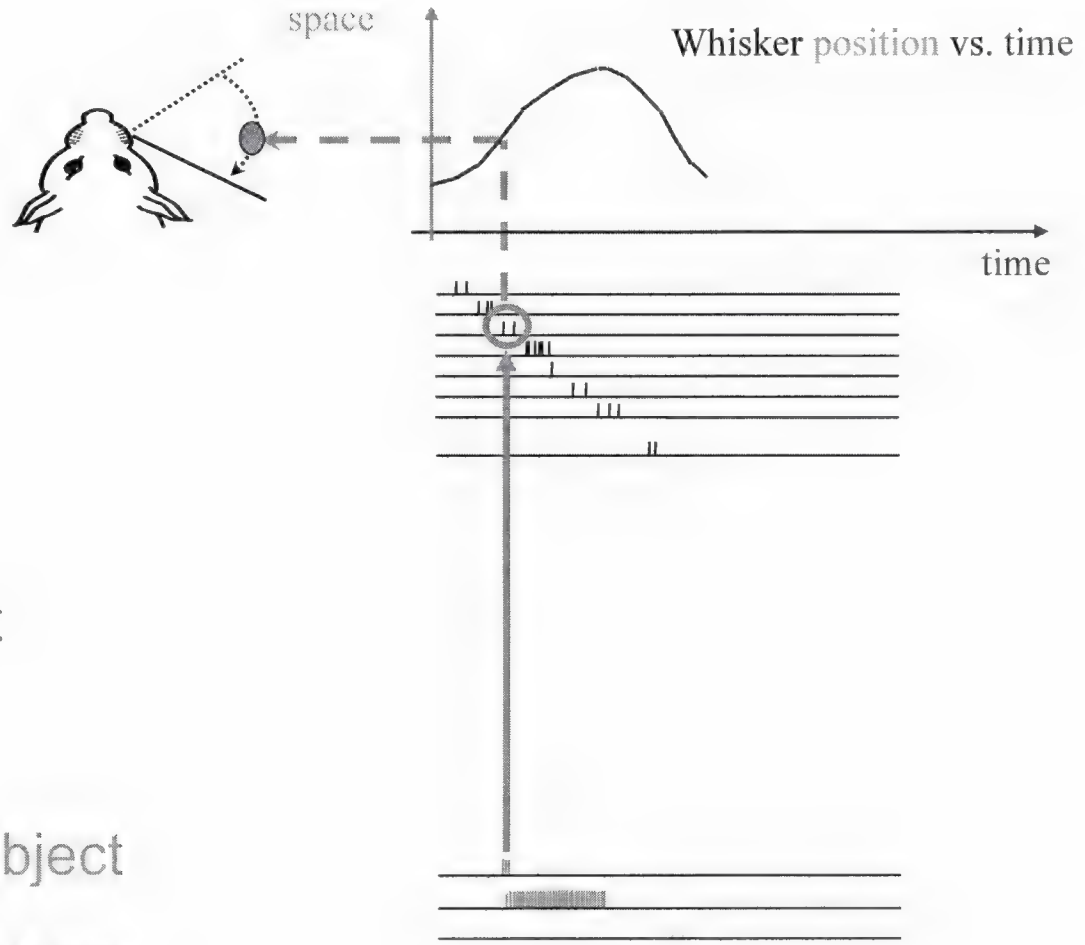
pressure against object

detachment from object



How can the brain extract the location of the object

- Whisking:



- Touch:

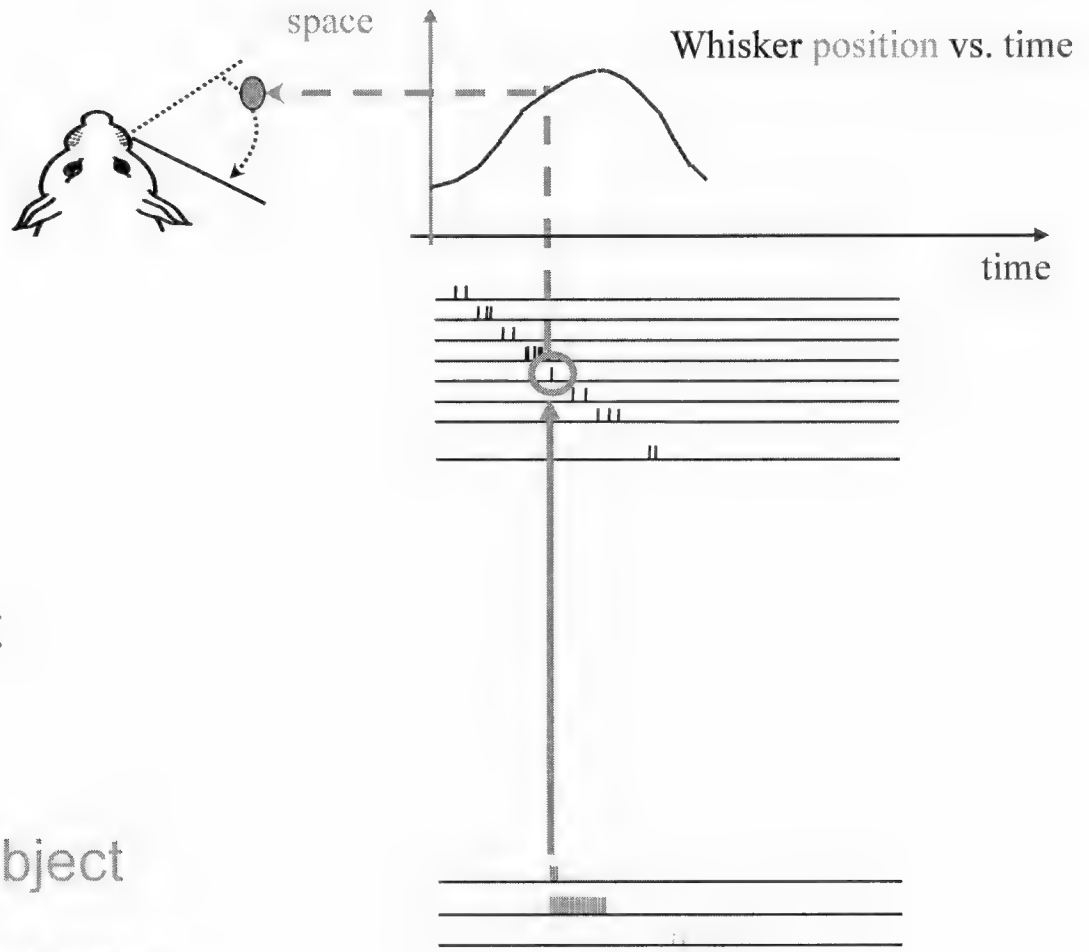
contact with object

pressure against object

detachment from object

How can the brain extract the location of the object

- Whisking:



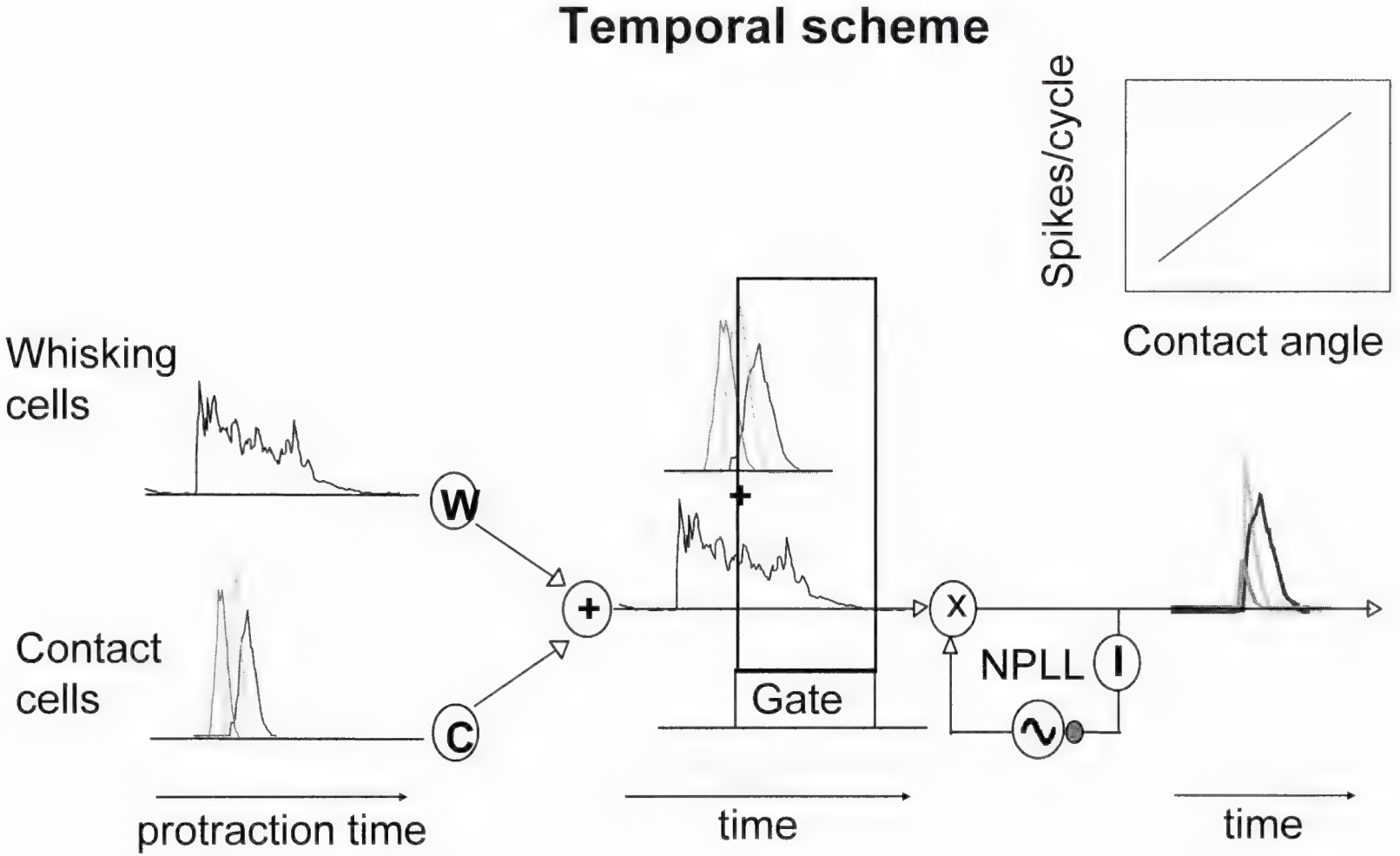
- Touch:

contact with object

pressure against object

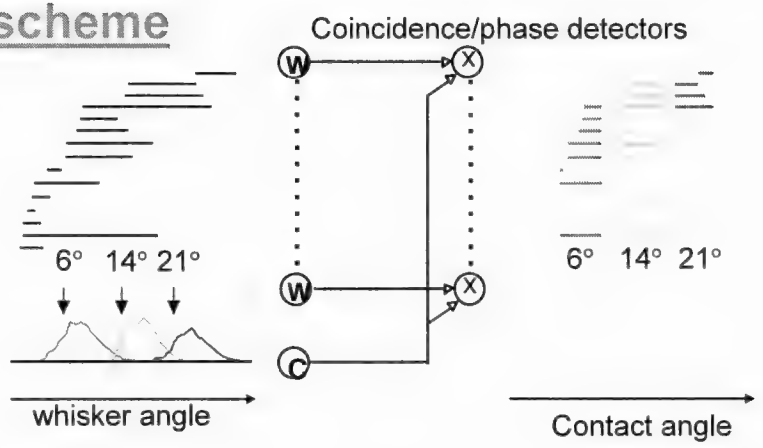
detachment from object

Encoding-decoding schemes

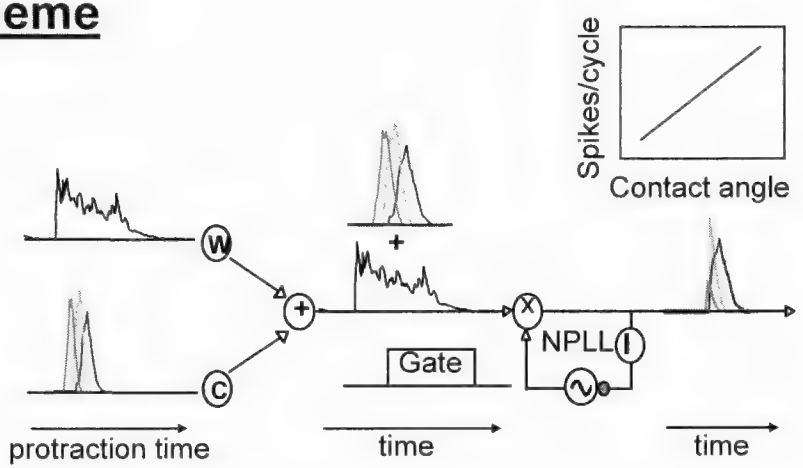


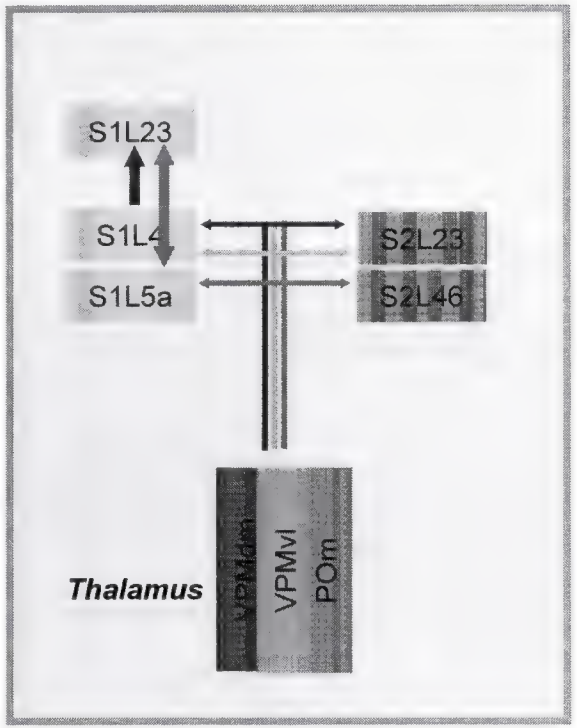
Encoding-decoding schemes

Spatio-temporal scheme

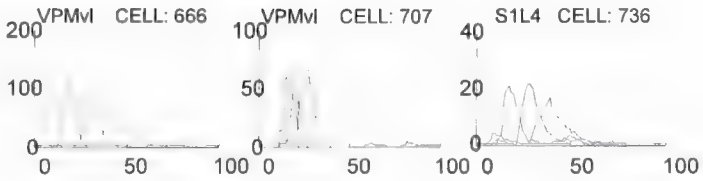


Temporal scheme

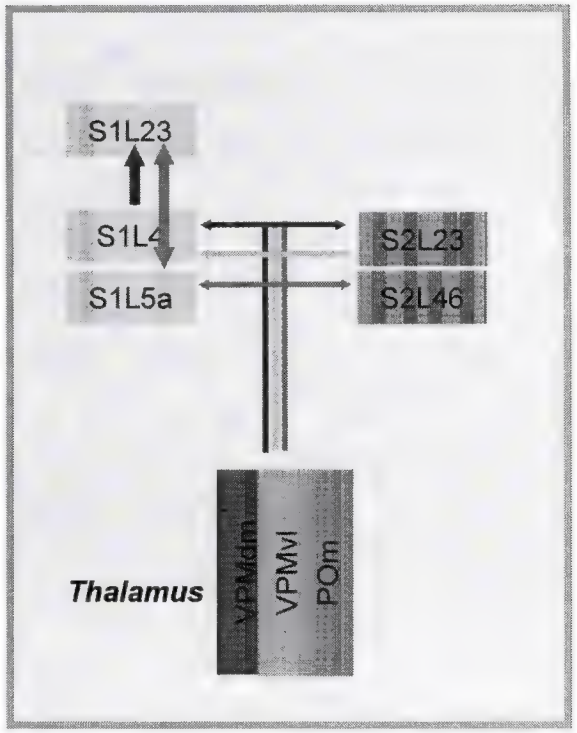


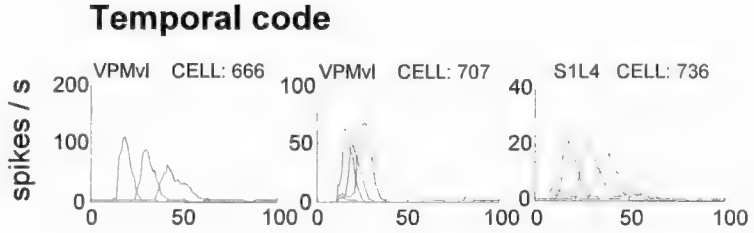


Temporal code

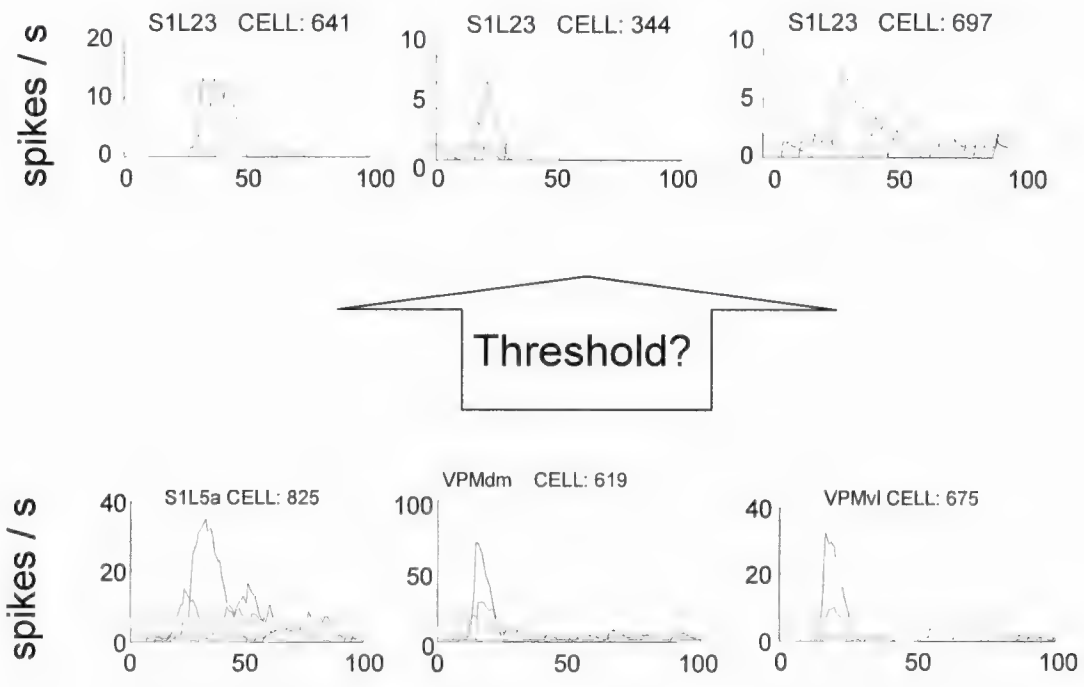


(Yu et al., unpublished)

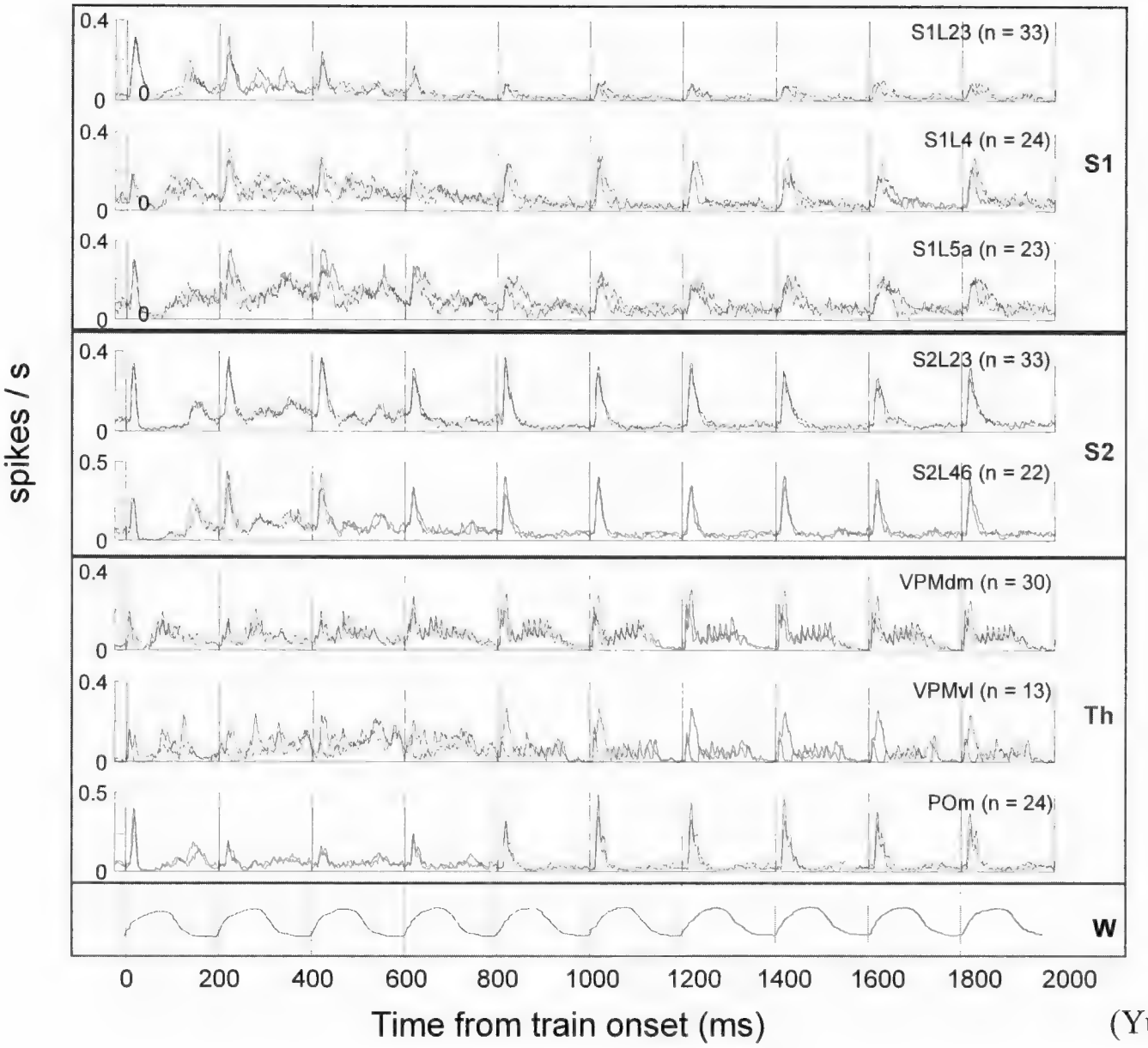




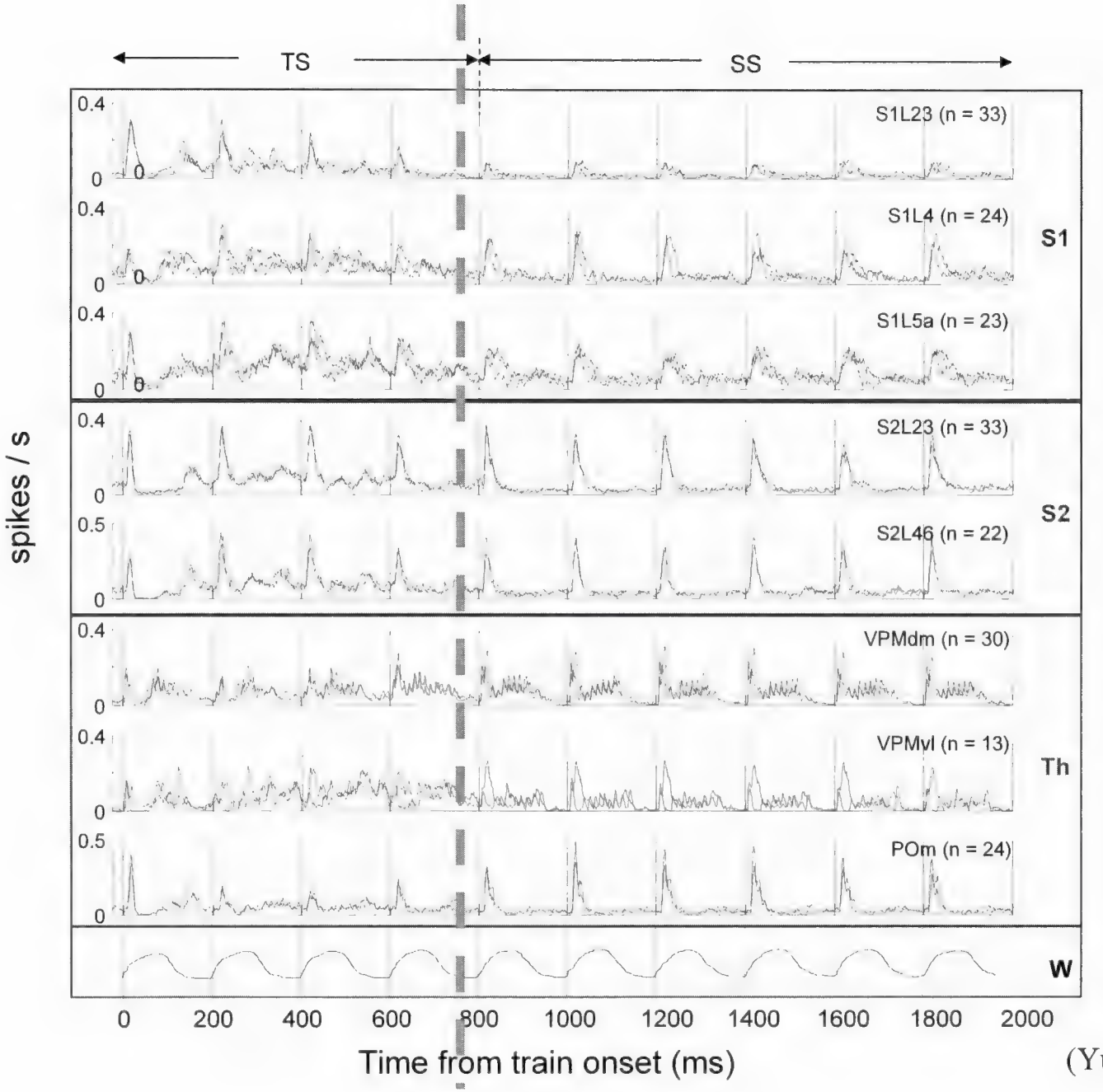
(Yu et al., unpublished)



(Yu et al., unpublished)

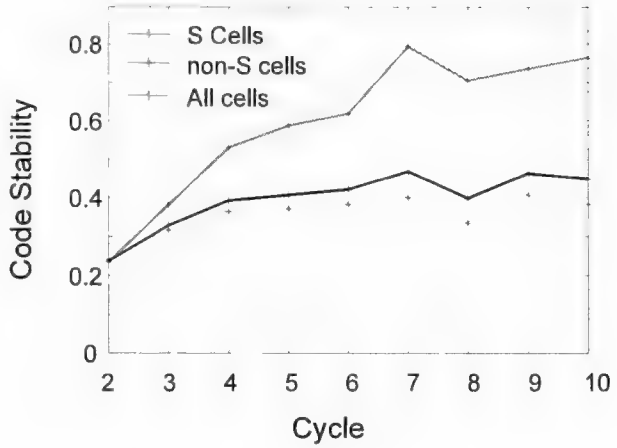


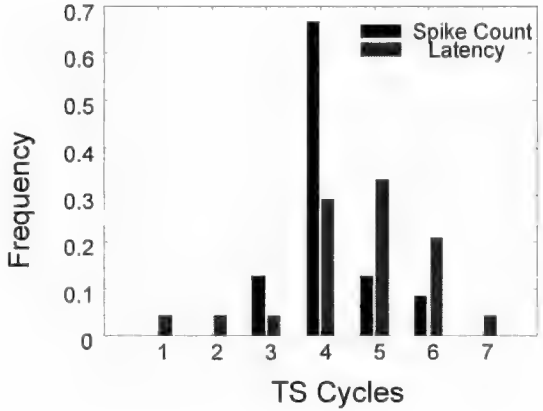
(Yu et al., unpublished)



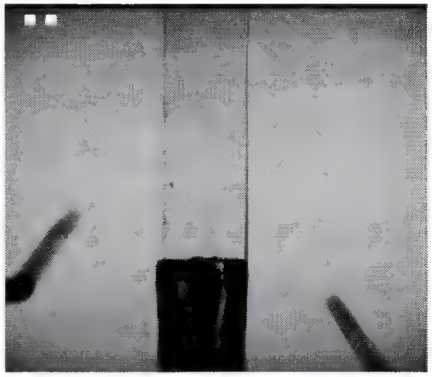
(Yu et al., unpublished)

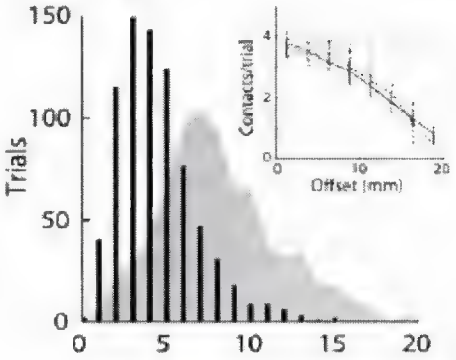
Anesthetized
artificial whisking





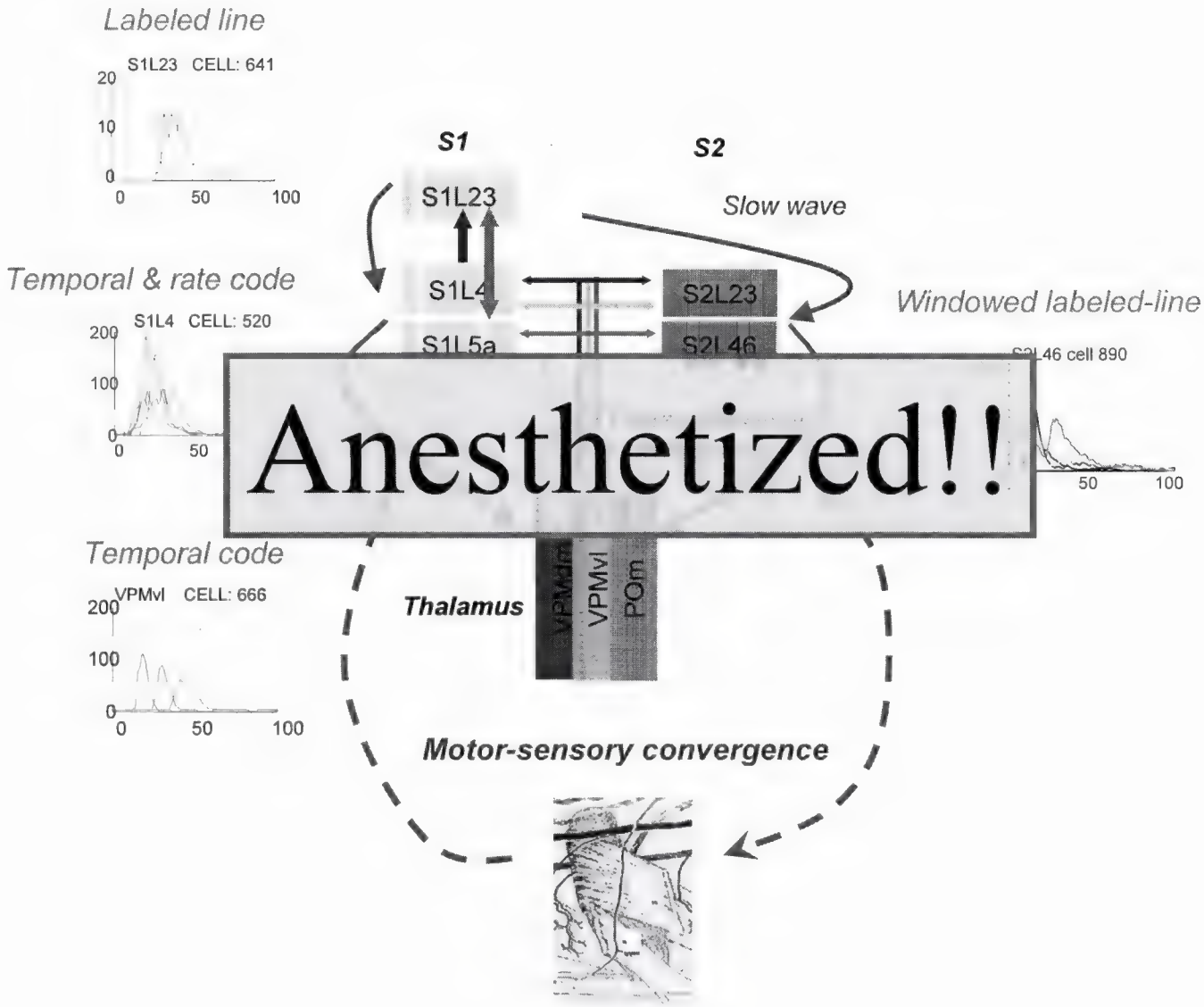
Behaving
natural whisking





(Knutsen et al, 2006)

(Yu et al., unpublished)


Labeled line
S1L23 CELL: 641
20
10
0
0
50
100
S1
S2
S1L23
Slow wave
Temporal & rate code
S1L4
S2L23
Windowed labeled-line
S1L4 CELL: 520
200
100
0
0
50
S1L5a
S2L46
S2L46 cell 890
50
100
Anesthetized!!
Temporal code
VPMvl CELL: 666
200
100
0
0
50
100
Thalamus
VPMdm
VPMvl
POm
Motor-sensory convergence

David...

Review

Cell PRESS

Orthogonal coding of object location

Per Magne Knutsen[1,2] and Ehud Ahissar[1]

[1] Department of Neurobiology, Weizmann Institute for Science, Rehovot 76100, Israel
[2] Department of Physics, University of California, San Diego, La Jolla, CA 92093, USA

It has been argued whether internal representations are encoded using a universal ('the neural code') or multiple codes. Here, we review a series of experiments that demonstrate that tactile encoding of object location via whisking employs an orthogonal, triple-code scheme. Rats, and other rodents, actively move the whiskers back and forth to localize and identify objects. Neural recordings from primary sensory afferents, along with behavioral observations, demonstrate that vertical coordinates of contacted objects are encoded by the identity of activated afferents, horizontal coordinates by the timing of activation and radial coordinates by the intensity of activation. Because these codes are mutually independent, the three-dimensional location of an object could, in principle, be encoded by individual afferents during single whisker–object contacts. One advantage of such a same-neuron-different-codes scheme over the traditionally assumed same-code-different-neurons scheme is a reduction of code ambiguity that, in turn, simplifies decoding circuits.

Introduction

Twenty years ago, the question 'what is the neural code?' was frequently heard in the corridors of neuroscience departments. Unlike the genetic code, which maps specific tri-nucleotide sequences to specific amino acids, no single neural variable has been found that consistently maps specific activity patterns to specific internal representations. Moreover, research conducted during the past twenty years indicates that the aforementioned question is ill-posed because well-posed coding questions should specify the external coded quality, the encoding system and the neuronal level in that system.

Neural codes for specific qualities, systems and levels range from the simple to the complex. In some cases, the presence of action potentials unequivocally signals a specific stimulus, such as a noxious one. More typically, however, action potentials additionally encode the intensity, timing or spatial characteristics of a stimulus. In principle, different attributes of external objects can be encoded, at each neuronal level of a given sensory system, by different neurons using the same code, by the same neurons using different codes or by different neurons using different codes.

Here, we review recent advances in understanding how primary afferents of the rodent vibrissal (whisker) system encode the three-dimensional location of objects. Sensory information from a single whisker enters the nervous system via 200–400 afferents that are activated when the whisker is actively moved or contacts an object. After contact, the whisker bends and vibrates [1], activating mechanoreceptors within the whisker follicle [2]. By recording the activation of individual primary afferents when the whisker is moved in a controlled but naturalistic manner in anesthetized rats, and monitoring whisker movements and performance of rats during localization of objects, we have begun to understand the principles of neural coding in the vibrissal system. Here, we review evidence that primary afferents of the vibrissal system employ an orthogonal coding scheme to represent the location of objects.

Principles of encoding object location

Rats possess a specialized system for active touch. The mystacial pad contains ~35 large whiskers (vibrissae) arranged in five rows and seven columns (Figure 1). One salient function of the whiskers is object localization. By sweeping their whiskers back and forth at rates of 5–20 Hz, rats efficiently scan the environment and localize objects within a few whisking cycles [3–5]. The location of an object, or whisker, can be represented in several coordinate systems. Here, we primarily refer to head- and whisker-related Cartesian or spherical coordinates (Box 1). Cartesian coordinates are specified by three spatially orthogonal axes: the (i) rostrocaudal (horizontal), (ii) dorsoventral (vertical) and (iii) mediolateral (radial) axes. Spherical object coordinates are specified in terms of azimuth, elevation and radial distance. Transformations between these coordinate frames are straightforward (Box 1) and we discuss encoding in both in parallel.

In principle, the coordinate of an object along each axis could be represented by different neural codes, each belonging to a different encoding domain. Four such domains are space, intensity, time and posture. Spatial encoding is based on the distribution of activated sensory neurons, intensity coding on the amount of sensory activation, temporal coding on the timing of activation, and posture coding on whisker posture during contact. Additionally, different combinations, or derivatives, of these variables could encode object location.

The simplest implementation of a spatial code is coding by neuron identity, known as a 'labeled-line' scheme, in which every neuron is associated with one sensory event. During object localization, labeled-line coding assumes that a specific cell is exclusively activated when an object is contacted at a particular location. Because primary sensory neurons are connected to only one whisker, these cells do encode the identities of the whiskers that contact an object. Thus, if the identity of contacting whiskers relates to object location, primary neurons will encode

Corresponding author: Ahissar, E. (ehud.ahissar@weizmann.ac.il).

0166-2236/$ – see front matter © 2008 Elsevier Ltd. All rights reserved. doi:10.1016/j.tins.2008.10.002 Available online 13 December 2008

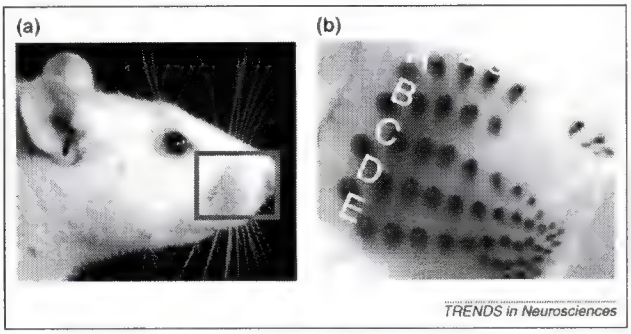


Figure 1. **(a)** The whiskers of the rat mystacial pad (red rectangle) are organized in **(b)** five rows (A–E) and four or more arcs [38]. Four stragglers appear to the left of the letters.

Box 1. Coordinates of whisker orientation and object location

Several body parts are involved in positioning the whiskers in space, including the body, head, mystacial pad and the whiskers' follicles. Each of these can be rotated or translated by a specific set of muscles and according to a specific frame of coordinates. Transformations between one coordinate frame to another are required when external objects, localized by one system (e.g. whisker), are approached by another system (e.g. mouth). Figure I describes coordinates of whiskers and external objects in two coordinate frames: whisker related and head related.

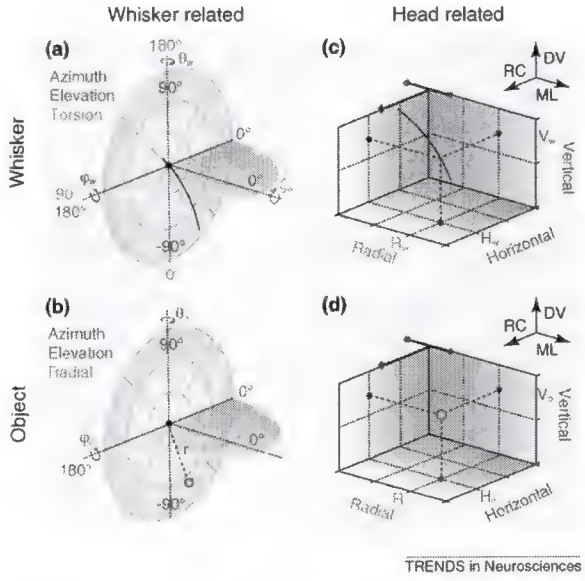


Figure I. **(a)** Whisker coordinates in a spherical, whisker-related reference frame. The orientation of a whisker in space can be described relative to its virtual pivot point (black dot at the origin) by the spherical coordinates azimuth θ (magenta), elevation φ (green) and torsional angle ζ (blue) [15]. (b) Object coordinates in a whisker-related reference frame. The position of an external object (purple ball) can also be described in spherical whisker-related coordinates, but with the radial distance from the pivot point replacing torsional angle. (c-d) Whisker and object coordinates in a Cartesian, head-related reference frame. The position of any point along the whisker shaft (c), or that of an object (d), can be described relative to the head, indicated here by the position of the eyes (red dots) and nose (red diamond) and by its horizontal (rostro-caudal; H), vertical (dorso-ventral; V) and radial (medio-lateral; R) coordinates. Subscripts denote whether the angles or positions refer to whisker (*w*) or object (*o*) coordinates.

location by labeled lines. This is illustrated in Figure 2, which demonstrates different encoding schemes when a realistically sized whisker array protracts from a typical resting angle and encounters a small object at the height of row C. When all whiskers synchronously protract, only whiskers in the row at the same elevation as the object can contact the object. The resulting identities of contacting whiskers, thus, reliably encode the elevation of the object (Figure 2e). Additional information about the position of an object can be derived from the intensity of sensory activation. In its simplest form, the intensity code is again a labeled-line, binary code; afferents fire if, and only if, contact intensity (velocity change or bending) passes a certain threshold. More likely, however, is that afferents respond with a rate function; higher contact intensity result in more spikes being emitted by the afferents [6]. Coding of object position by intensity is illustrated in Figure 2f, in which sensory activation is assumed to be proportional to the degree of protraction upon contact. In this scenario, the azimuth of the least-protracted contacting whisker (C2) is closest to the azimuth of the object owing to bending of the other contacting whiskers with greater azimuths. Thus, the order of sensory-activation magnitude can map space and action onto different activity levels; the further protracted the whiskers or the closer the object along the horizontal axis, the more intense the sensory activation will be.

Spatial and intensity codes are limited in how accurately they can represent object location because these are discrete codes; spatial codes are carried by individual primary afferents, of which there is a finite number, and intensity codes by discrete spike events. The resolution of such codes can be extended by interpolating across space and intensity (e.g. between activity levels of neighboring whiskers) or by integrating the activity of many afferents. Temporal codes, however, are measured along a continuum and, thus, have potentially higher resolution. Indeed, temporal codes encode stimuli with sub-millisecond precision along the trigeminal pathway [7–9]. Because the whiskers move, the timing of whisker–object contacts and, thus, the timing of afferent activation encodes object position (Figure 2g). Relative to other reference events (such as the position signal in Figure 2d, internally generated or mechanoreceptor derived) these temporal events encode the coordinate of the object along the movement axis.

The intensity and temporal codes in Figure 2 depend on motor variables. Motor or proprioceptive signals that indicate whisker posture (e.g. azimuth; Figure 2d) can also encode object location when taking into account contact timing and whisker morphology.

Response characteristics of primary vibrissal afferents

The vibrissal system is composed of many nested motor-sensory loops [10]. This architecture enables rats to dynamically control whisker movement [4,11–16], which rats exploit when performing different tasks [3,5,17]. Although beneficial for the rat, such dynamic control renders successive contacts different from each other [4], which prevents systematic investigation of sensory signals during object localization. To systematically study sensory signals

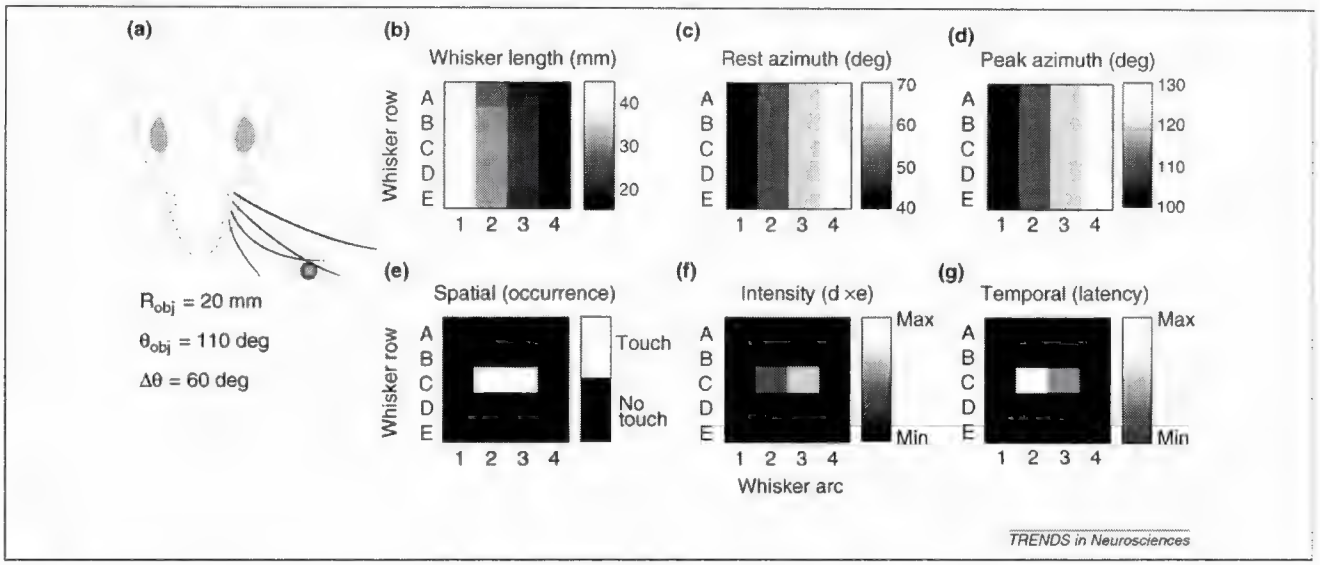


Figure 2. Object location in a head-centered reference frame represented through different encoding schemes. **(a)** During a typical whisking cycle, the whisker field protracts synchronously, here represented by four whiskers in row C. **(b)** The length distribution of whiskers drops approximately linear along arcs [39]. **(c)** In this illustration, all whiskers were assumed to protract 60 degrees (deg) azimuthally from different rest angles to the most protracted positions in **(d)**. **(e–g)** The effects of contact with a point object for individual whiskers were simulated for different encoding schemes during peak protraction. The object was positioned at a radial coordinate (R_{obj}) of 20 mm, 110 deg azimuth and at the vertical level of whisker row C. (e) Coding by identity: during maximal protraction of the whole whisker field, only whiskers C2 and C3 contacted the object. (f) Coding by intensity: the intensity of the contact was estimated by multiplying the identity matrix in (e) by the whisker position matrix in (d). (g) Coding by timing: the order in which whiskers C2 and C3 contacted the object corresponds to a temporal code.

induced by muscle-driven contact, Bagdasarian and colleagues* eliminated the operation of motor-sensory loops by anesthetizing rats and electrically stimulating the distal segment of a transected motor nerve (Figure 3a) to mimic natural whisker movements [18,19]. This paradigm deviates from classical paradigms using passive whisker deflections (Box 2). During passive movement, mechanoreceptors are activated by external forces applied to the whisker. During active movement, however, mechanoreceptors are activated both by forces owing to muscle protraction and reaction forces generated when whiskers contact objects. This difference leads to significantly different response characteristics of primary vibrissal afferents in the trigeminal ganglion (TG). During passive stimulation, TG cells are selective for deflection direction and velocity and can be characterized as slowly or rapidly adapting [18,20]. During active touch, TG neurons can be grouped into four major categories based on their response characteristics during whisking and touch [19]: contact, pressure, detach and whisking. Contact cells respond briefly and with short latency after a whisker contacts an object (Figure 3b). Pressure cells respond for as long as contact is maintained (Figure 3c). Detach cells respond only when the whisker detaches from the object (Figure 3d). Collectively, contact, pressure and detach cells are referred to as touch cells. The fourth class, whisking cells, respond to movement (Figure 3e) and are not affected by the presence of objects in the distal part of the whisking field; the sensitivity of these neurons to proximal contacts (<50% of whisker length) has not yet been tested. An additional class of cells (whisking/touch) respond during whisking and increase their firing upon and during touch [19].

Encoding object location with primary afferents

Using artificial whisking, Szwed and colleagues studied how TG neurons encode object position during active touch [19,21]. Encoding of the horizontal coordinate was studied by varying the azimuth angle of an object (θ_{obj}) within the movement trajectory of a whisker (Figure 4a). Touch-responsive cells (primarily contact cells) reliably encode the azimuth angle of the object by the latency from protraction onset to the first emitted spike in a whisking cycle [19], but not by spike count or spiking rate (Figure 4b,c). In order for a temporal code (such as spike latency) to be meaningful, read-out circuits must compare it with a reference signal such as an internal motor copy. A precise reference signal is the re-afferent information signaled by whisking cells (Figure 3e), whose activity is locked to specific phases of the movement cycle [19]. Thus, the azimuth angle of objects can be encoded by the relative timing of TG whisking and touch signals and, later, read out by circuits receiving both signals. The location and exact mechanism of the decoding circuit(s) is unknown; available data indicate that such circuits function downstream to the thalamus [22] and involve the somatosensory cortex†.

Unlike horizontal location, the radial coordinate of objects seems to be encoded by several neuronal variables, the primary being the spike rate of touch cells. When an object is positioned at increasing radial distances (Figure 4d), most touch cells respond with a decreasing

* Bagdasarian, K. *et al.* (2002) Encoding of radial object position by rat whiskers: recordings from the trigeminal ganglion. *FENS Abstr.* 1, A052.3.

† Curtis, J.C. and Kleinfeld, D. (2006) Confluence of position and active touch in rat primary somatosensory cortex. *Soc. Neurosci. Abstr.* 32, 144–3.

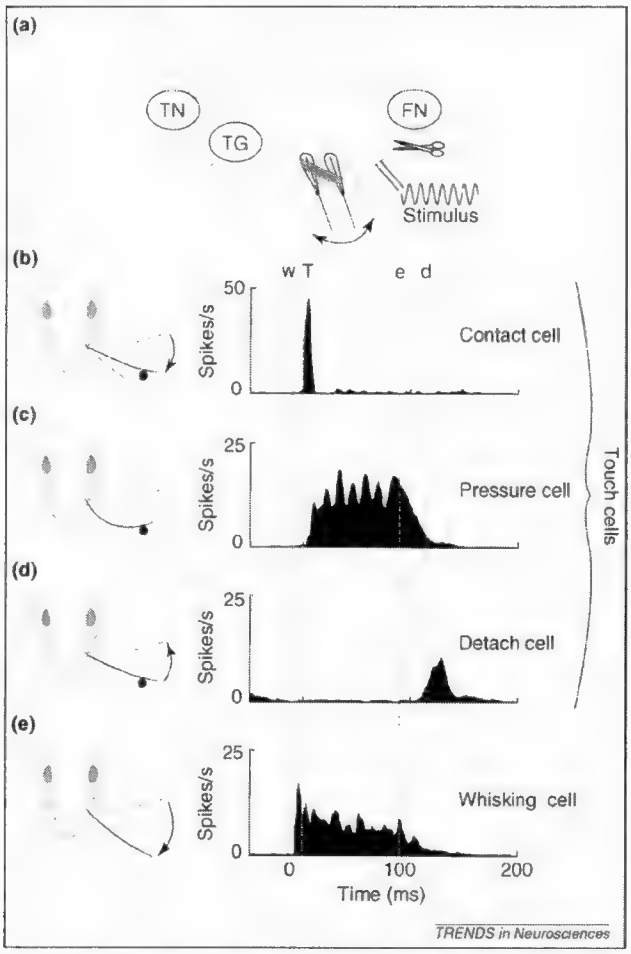


Figure 3. **(a)** Method for artificially inducing whisker movements in the anesthetized rat. Sensory-motor feedback was cancelled by cutting the facial motor (VII) nerve, and whisker movements were controlled by electrically stimulating the distal segment of the nerve [19]. Solid lines indicate known connection and dotted lines indirect connections between trigeminal nuclei (TN) and facial nucleus (FN). During artificial whisking, an object was placed at different locations within the movement path. The most important events in each cycle with the object present (indicated by letters above dashed lines) were onset of movement (w), contact with the object (T), end of stimulation and whisker protraction (denoted with the letter e) and detach of the whisker shaft from the object (denoted with the letter d). TG neurons were grouped into four classes based on response characteristics to these events. **(b)** Contact cells responded only briefly to contact, but not to any other event. **(c)** Pressure cells responded to contact for as long as contact was maintained. **(d)** Detach cells responded only to object detaches. **(e)** Whisking cells responded to whisker movement and were not affected by object contact or detach. The whisking response was present regardless of the presence or absence of the object. Responses of a subpopulation of cells responding to whisker movement were augmented by object contact (whisking/touch cells, not shown). Adapted from Refs [19,21]. Abbreviations: FN, facial nucleus; TG, trigeminal ganglion; TN, trigeminal nuclei.

number of spikes per movement cycle [21] (Figure 4e,f). Other cells encode radial location by distinct thresholds and respond exclusively when the object is positioned at very proximal radial locations. Given the considerable variability between individual cells in their ability to encode radial location and the existence of cells that do not exhibit monotonic dependence on radial position [21], read-out mechanisms for radial location should be based on input from populations of touch cells rather than on individual cells.

The movement direction of the whiskers is along the plane of rows [15,23]. This, and the fact that TG neurons always have single-whisker receptive fields [24], dictates that when a TG neuron is activated an object must have been present at the elevation of the row the whisker belongs to. Thus, the vertical coordinate of contact is encoded by neuron identity (Figure 1e).

Behavior and performance during object localization

The ability of rats to localize objects, the motor strategies employed and the conditions for localizing along horizontal and radial dimensions has been studied by isolating spatial dimensions and removing sub-sets of whiskers [3,5,25–27]. Such behavioral studies support neuronal-driven hypotheses of how object location is encoded. Knutsen *et al.* [3] trained rats to discriminate the relative horizontal location of two objects (Figure 5a). The ability of the rats to perform such discriminations was correlated with the initial whisker-array configuration used during learning of the task and the amount of whisking, as measured by the spectral power of whisking (Figure 5b). Rats could localize with a single whisker intact on either side of the snout, but only if the rats had initially been trained with multiple whiskers intact. Both with multiple or single whiskers intact, rats reached hyperacuity resolution. That is, rats could localize with a resolution (1–5°) significantly better than the limit imposed by the spacing of adjacent same-row whiskers (~20°) [3]. Such performance levels preclude encoding of horizontal location by whisker identity. Instead, the correlation between localization acuity and whisking power indicates that temporal events associated with whisker movement are, as expected from primary afferent responses, important for encoding the horizontal dimension. Indeed, the same study showed that rats that were unable to move their whiskers during discrimination, except through the use of head movements, after bilateral lesions of the facial motor nerves were unable to discriminate horizontal offsets between objects (Figure 5b). In a similar study, hyperacuity performance was not achieved when rats had to determine the horizontal coordinate of a single object without a reference to a second, simultaneously presented object [5]. In such an absolute localization task, which is in essence memory guided, localization acuity (~15°) drops to the order of the typical inter-whisker spacing. In an analogy, visual hyperacuity (~0.001°) is only achieved when stimuli are localized relative to each other and not when stimuli need to be localized in space without a reference, in which case acuity drops to ~0.01° (i.e. to the order of photoreceptor spacing [28]).

The ability of rats to localize features along the radial dimension has been studied during absolute and relative discriminations. In an absolute, memory-guided task, Krupa and colleagues [26] trained rats to discriminate apertures with varying radial widths as either 'narrow' or 'wide'. In a variation of this task, Schuler *et al.* [27] trained rats to make relative, bilateral discriminations and judge the two walls of the apertures as 'equidistant' or 'non-equidistant' (Figure 5c). During performance of both tasks, whisking was absent and whiskers brought in contact with the walls primarily through head and body movements. Performance during absolute radial localization was reliable even after complete facial motor-nerve lesions

Box 2. Active versus passive touch

During naturally, self-generated whisking by freely-moving animals, both whisker protraction and retraction are active and controlled by groups of intrinsic and extrinsic muscles [11,40]. Forces, thus, act directly on the whisker follicles both upon contact and detach with an object (Figure Ia). Upon contact with an object (blue sphere), contacting whiskers bend as a function of whisker material properties, head-position, muscle forces and object location. Thus, not every contact yields identical whisker curvatures. How rats exploit this to encode object position is unknown because response features of primary afferents in behaving animals have not yet been characterized. Clues to how afferents encode object position can be obtained from artificially whisking anesthetized rats. Artificial whisking is generated by electrically activating the facial motor nerve [19]* (Figure Ib). This method activates all muscles simultaneously and, thus, does not preserve the normal phase relationship between muscles associated with protraction or retraction [11]. The net outcome of artificial whisking is protraction, although the detailed motions differ somewhat from self-generated whisking. As occurs during self-generated whisking, whiskers bend upon contact with an object, and both muscular and object induced forces are applied to the follicle-whisker complex. During these conditions, primary afferents exhibit selectivity for either touch or whisking, or both [19].

A common technique for probing afferent activity, which ignores the active nature of vibrissal touch, is deflections of passive, stationary whiskers using mechanical stimulators or air pressure. During such stimulation, no muscles are activated and the whisker is merely deflected from its resting position (Figure Ic). Thus, passive stimulation only mimics the forces applied to the whisker shaft during contact. As a result, the induced mechanical changes are different. For example, passive deflections induce curvature and angle changes in opposite directions, whereas active touch induces curvature and angle changes in the same direction. Owing to these mechanical differences, neural selectivity revealed during active and passive touch is qualitatively different and usually cannot be deduced from each other even when the same neuron is recorded in both conditions [19,21,41,42].

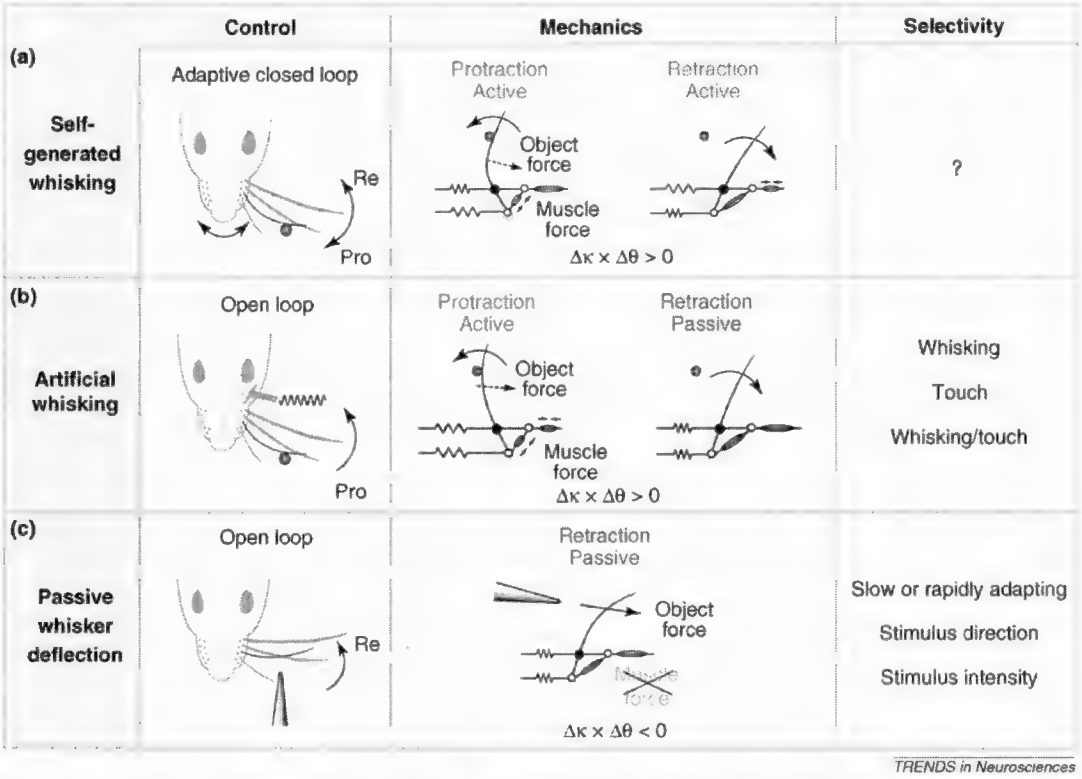


Figure I. Three different paradigms of whisker stimulation and the resulting mechanics and neuronal activity. **(a)** During self-generated whisking, both muscle and contact forces influence whisker mechanics. The neuronal activity of individual primary afferents during such stimulation is unknown (denoted ?). **(b)** Artificial whisking evoked by direct motor-nerve stimulation enables experimental control of active whisking but does not fully reproduce all aspects of normal behavior. Retraction is initiated by cessation of electrical stimulation and is therefore passive, whereas during self-generated whisking dedicated muscles contribute to fast whisker retraction. Neuronal activity during artificial whisking is highly selective to specific events within the whisk cycle, such as contact and motion. **(c)** Passive deflection is the most utilized method of whisker stimulation. During passive deflection, muscle contraction is absent and neuronal selectivity is delineated as a function of adaptation time constants, directional tuning and stimulation intensity thresholds. In the left column, Pro and Re denote protraction and retraction, respectively. In the middle column $\Delta\kappa$ denotes the induced change in whisker curvature and $\Delta\theta$ the induced change in whisker angle.

(Figure 5d). Performance, however, was significantly affected by the number of intact whiskers available to the rat, although it did not depend on the identity of contacting whiskers [26] (Figure 5d). The fact that whisker movements were not required, and typically not present during radial localization, indicates that temporal cues are not important for radial localization. Furthermore, simple spatial codes, such as a labeled-line code, can be ruled out because the identities of intact whiskers were not a determining factor for performance. Although measurements of localization acuity were not an explicit objective in the relative radial discrimination study, stable performance (86% correct) was reported only at a radial offset of 11 mm [27]. In the absolute radial discrimination task, rats were capable of discriminating aperture widths as small as 3 mm [26]. Thus, a similar advantage as that conferred

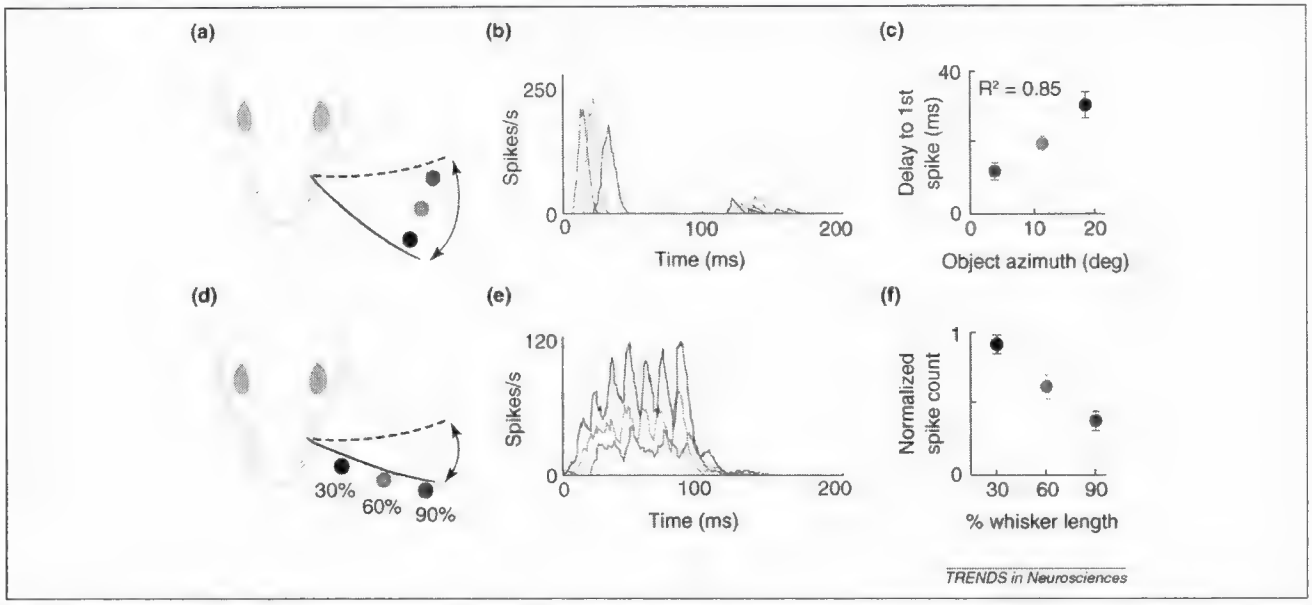


Figure 4. (a-c) Touch cells encode the horizontal location of objects. Artificial whisking was induced in anesthetized rats and an object placed at different azimuth angles. Touch cells reliably encoded object azimuth by increasing latency to the first spike with increasing object angle. Average response latencies shown in (c) are for a single touch cell. (d-f) Pressure cells encode the radial location of objects. Pressure neurons encoded the radial location by reducing the net spike count during protraction as the radial location became more proximal. The correlation between spike count and radial location shown in (f) include all recorded pressure cells ($n = 38$). Adapted from Refs [19,21].

by making simultaneous comparisons between two objects during horizontal localization [3] has not been demonstrated for radial localization. This might be related to the coding scheme used in each case. When sensory acuity depends on movement-dependent temporal cues, acuity can be improved by controlling whisker movements. The actual motor patterns used to acquire the high-resolution data, however, might not be stored in memory and will, thus, not be available for comparisons during absolute horizontal localization. By contrast, sensory data that do not depend on sensor motion, such as population firing rates that seem to encode radial location, contain all necessary information for future comparisons, albeit with lower resolution.

Coding of different spatial dimensions use different neuronal variables and are optimized with compatible

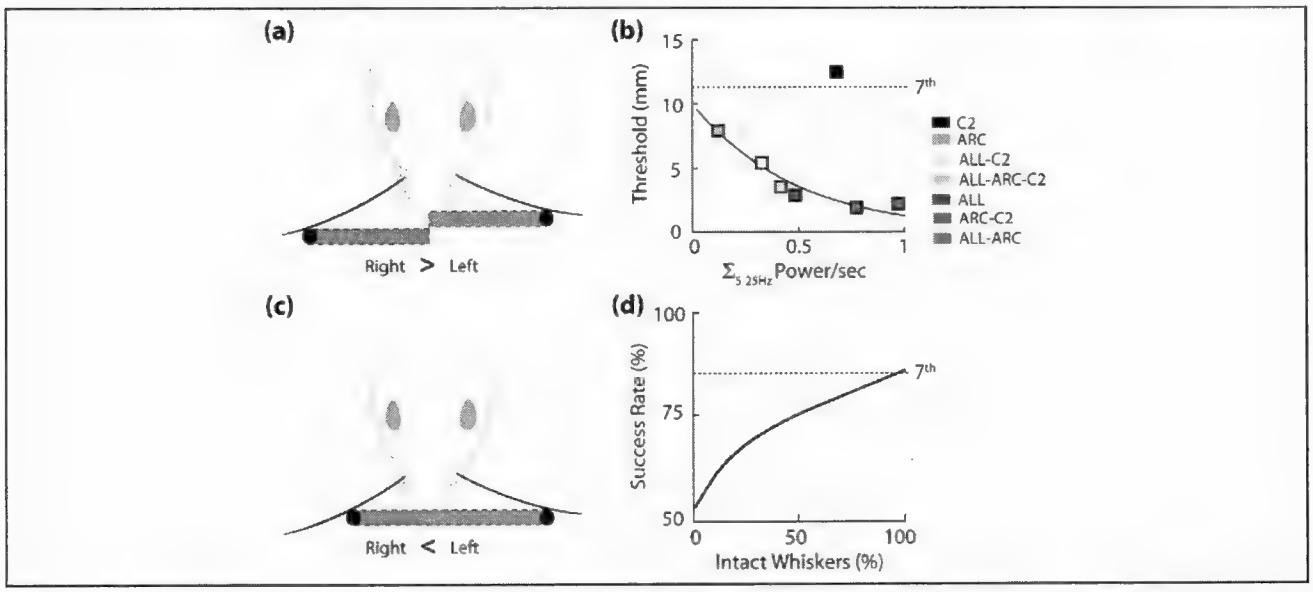


Figure 5. (a) Rats were trained to discriminate the relative horizontal offsets of two vertical poles (blue) [3]. (b) During horizontal object localization, performance did not depend on the number or identity of intact whiskers. Instead, performance was related to the order in which whisker-array configurations were exposed to the task and the amount of whisking executed during test trials. Rats with a single whisker intact are C2, those with an arc of whiskers intact are denoted ARC and those with all whiskers intact are denoted ALL. Colored squares denote the order of whisker-array configurations rats were exposed to. Lesioning the facial motor nerve reduced performance to chance level (dashed line). (c) Rats were trained to discriminate the radial offset between two bilaterally placed objects. The task variations included judging the objects as equidistant or non-equidistant (as shown) [26] or to detect the location of the 'near' or 'far' object (not shown) [27]. (d) Performance during the relative radial object localization was correlated with the number of intact whiskers. Lesioning the facial motor nerve did not affect radial localization performance (dashed line).

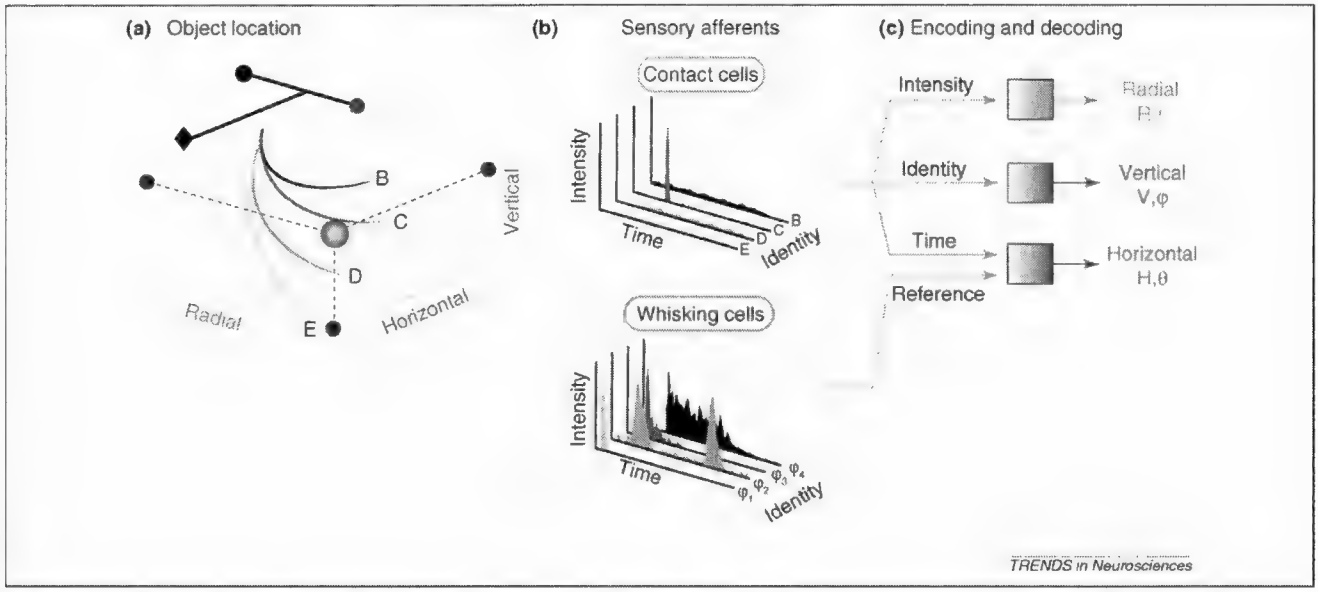


Figure 6. Orthogonal coding of object location. **(a)** Different whiskers (gray lines) interact with an object differently owing to their lengths or position on the whisker pad. Here, whiskers in rows B–E belonging to the same arc are shown in a protraction position, contacting an object at the level of row C (blue sphere). **(b)** During whisking and touch, the activation of whisking and contact primary afferents can be characterized by the identity of activated cells, the intensity of activation (firing rate or spike-count) and the timing of activation. The onset timing, or phase, of whisking cell activation is typically consistent for a given cell and location but varies across the whisking cell population (φ_1–φ_4). **(c)** When a contact primary afferent is activated, the whisker in its receptive field contacted an object. Because within any given whisking cycle a particular vertical coordinate is scanned only by a subset of whiskers, the firing of a contact primary afferent within that cycle indicates the elevation (vertical coordinate) of the object. The timing of the contact signal, relative to the firing timing of whisking afferents, indicates the azimuth (horizontal coordinate) of the object (Figure 4a–c). The net spike count emitted by the contact afferent during that cycle encodes the radial coordinate of the object (Figure 4d–f).

whisking strategies. Yet, during natural exploration, the location of an object in all three spatial dimensions must be encoded simultaneously to enable targeted actions. In nature, rats must optimize behavior simultaneously across all dimensions. Observations obtained to date indicate that dynamic movement control is probably the most readily available tool for rats to increase acuity in real time and is undoubtedly used by rats while solving challenging tasks.

Orthogonal encoding of object location

By combining the neuronal and behavioral observations reviewed earlier, we suggest the following encoding scheme for object localization during whisking (Figure 6). In both head- and whisker-centered coordinate schemes, the three orthogonal coordinates, horizontal, vertical and radial (θ, φ and r; H, V and R in Box 1), are encoded using three orthogonal neuronal codes: a spatial code for the vertical (elevation) coordinate, a temporal code for the horizontal (azimuth) coordinate and an intensity code for the radial distance. Intensity coding of radial position is likely to be based on interpolating firing intensity across multiple whiskers. Temporal encoding of horizontal position should use a comparison of contact time with a reference signal of a proprioceptive nature (meaning that the reference signal represents the motion of the whisker), such as (i) the timing of protraction onset or (ii) whisker position at the time of contact. Both these signals are conveyed by peripheral whisking neurons [19] and exist in the somatosensory thalamus [22] and somatosensory cortex [29–31]†.

In principle, individual TG touch neurons could convey information about the three coordinates simultaneously within one whisking cycle. The fact that particular touch cells are activated conveys information about the vertical coordinate of an object, the onset time of firing conveys information about the horizontal coordinate and the intensity of firing conveys information about the radial coordinate of an object (Figure 6). One feature of orthogonal coding is that the output signals of touch cells can be conveyed in parallel to different, specialized decoding (readout) circuits, each of which decodes a particular neural variable. Although the specific read-out mechanisms are yet to be discovered, already-known neural circuits could be used for decoding the signals of touch cells. The vertical coordinate can be read out by threshold detectors, the horizontal coordinate by phase-locked loops or phase detectors [19] and the radial distance by neural integrators, peak detectors, attractor neural networks or synfire chains. Orthogonal coding reduces the ambiguity of afferent signals and, thus, simplifies these decoding algorithms. Through evolution, algorithms can become optimized for decoding a particular variable without dedicating resources to discriminating between input afferents because readout circuits should be specific to a variable but not necessarily to a neuronal population.

Perceptual coding versus sensory coding: role of motor strategies

Perception is a motor-sensory process, in which motor strategies determine the type and quality of sensory data. Rodents modify their whisking patterns when challenged with different perceptual tasks. For example, for texture identification rats typically employ continuous scanning profiles [32,33], whereas during exploration they seem to employ a minimal impingement strategy by which they

contact obstacles with as many whiskers as possible with very light touch [4]. In whisking rodents, object localization is achieved via body, head and whisker movements [3,5,26]. Thus, the sensory coding scheme described here is only one component involved in the perceptual process of localization. Individual rats can use these sensory codes differently, depending on their motor strategy. For example, during horizontal position discrimination, some rats might employ synchronous bilateral whisking and use the time difference between left and right contacts as a primary cue for discrimination [3]. Other rats might instead contact synchronously on both sides and use the bilateral angular difference as the primary cue for discrimination. Evidently, whisker angle and contact time are crucial in both sensory-motor processes, but each serves as a perceptual cue only in one of the strategies and as a sensory-motor coordinator in the other.

Thus, sensory cues that serve perceptual comparisons are not necessarily the same cues that convey primary sensory data (where by primary sensory data we refer to the manner of receptor activation). Perceptual comparisons depend on motor strategies, which involve multiple levels of sensory-motor control loops encompassing body, head and whisker movements [10], whereas sensory data depend only on the peripheral level of vibrissal interaction with the external world. Thus, a perceptual coding scheme, unlike a sensory coding scheme, must include motor variables in its definition. These motor variables change from task to task and between exploration epochs and whisking cycles. Therefore, with active sensing, perceptual coding cannot be based on fixed internal representations. Rather, during active sensing, internal representations are always functions of both external features and motor activity.

Conclusive remarks

Neuronal recordings in anesthetized rats and behavioral observations in rats performing localization tasks indicate that the vibrissal sensory organs implement an orthogonal coding scheme to encode object location: spatial coding for vertical coordinates, temporal for horizontal and intensity for radial coordinates. The decoding of object location by internal circuits must consider whisker reference signals. As several motor-sensory strategies can potentially be employed, examination of decoding algorithms should involve awake behaving animals [31–36]†. Furthermore, other potential encoding schemes must be examined in more detail. For instance, high-threshold afferents might additionally encode radial location by a labeled-line code [21], and it has been suggested that horizontal location might also be encoded, in part, by a labeled-line code owing to interactions between torsional whisker rotation and directional tuning of afferents [15]. A common requirement for several of the identified, putative codes is active sensing via whisking. The closed-loop architecture of the vibrissal system enables efficient adaptive control of vibrissal touch [4,37]. It remains to be seen to what extent adaptive behavior is, indeed, manifested during perceptual tasks, which motor variables are controlled in given contexts and how they are controlled. Improving our understanding of adaptive behavior will also facilitate our understanding of how tactile perception emerges during active sensing.

Acknowledgements

Work in the Ahissar laboratory is supported by the Israel Science Foundation (www.isf.org.il), the Minerva Foundation (www.minerva.mpg.de) funded by the Federal German Ministry for Education and Research, the United States-Israel Binational Science Foundation (www.bsf.org.il), the Human Frontiers Science Program (www.hfsp.org) and the EU FP7 BIOTACT project (ICT-215910; www.biotact.org). P.M.K. is a Human Frontier Science Program Long-Term Fellow. E.A. holds the Helen Diller Family Professorial Chair of Neurobiology.

References

1 Hipp, J. *et al.* (2006) Texture signals in whisker vibrations. *J. Neurophysiol.* 95, 1792–1799
2 Ebara, S. *et al.* (2002) Similarities and differences in the innervation of mystacial vibrissal follicle-sinus complexes in the rat and cat: a confocal microscopic study. *J. Comp. Neurol.* 449, 103–119
3 Knutsen, P.M. *et al.* (2006) Haptic object localization in the vibrissal system: behavior and performance. *J. Neurosci.* 26, 8451–8464
4 Mitchinson, B. *et al.* (2007) Feedback control in active sensing: rat exploratory whisking is modulated by environmental contact. *Proc. Biol. Sci.* 274, 1035–1041
5 Mehta, S.B. *et al.* (2007) Active spatial perception in the vibrissa scanning sensorimotor system. *PLoS Biol.* 5, e15
6 Gibson, J.M. and Welker, W.I. (1983) Quantitative studies of stimulus coding in first-order vibrissa afferents of rats. 1. Receptive field properties and threshold distributions. *Somatosens. Res.* 1, 51–67
7 Montemurro, M.A. *et al.* (2007) Role of precise spike timing in coding of dynamic vibrissa stimuli in somatosensory thalamus. *J. Neurophysiol.* 98, 1871–1882
8 Jones, L.M. *et al.* (2004) Precise temporal responses in whisker trigeminal neurons. *J. Neurophysiol.* 92, 665–668
9 Arabzadeh, E. *et al.* (2005) Neuronal encoding of texture in the whisker sensory pathway. *PLoS Biol.* 3, e17
10 Kleinfeld, D. *et al.* (2006) Active sensation: insights from the rodent vibrissa sensorimotor system. *Curr. Opin. Neurobiol.* 16, 435–444
11 Hill, D.N. *et al.* (2008) Biomechanics of the vibrissa motor plant in rat: rhythmic whisking consists of triphasic neuromuscular activity. *J. Neurosci.* 28, 3438–3455
12 Herfst, L.J. and Brecht, M. (2008) Whisker movements evoked by stimulation of single motor neurons in the facial nucleus of the rat. *J. Neurophysiol.* 99, 2821–2832
13 Cramer, N.P. and Keller, A. (2006) Cortical control of a whisking central pattern generator. *J. Neurophysiol.* 96, 209–217
14 Towal, R.B. and Hartmann, M.J. (2008) Variability in velocity profiles during free air whisking behavior of unrestrained rats. *J. Neurophysiol.* 100, 740–752
15 Knutsen, P.M. *et al.* (2008) Vibrissal kinematics in 3D: tight coupling of azimuth, elevation, and torsion across different whisking modes. *Neuron* 59, 35–42
16 Haiss, F. and Schwarz, C. (2005) Spatial segregation of different modes of movement control in the whisker representation of rat primary motor cortex. *J. Neurosci.* 25, 1579–1587
17 Sachdev, R.N. *et al.* (2003) Unilateral vibrissa contact: changes in amplitude but not timing of rhythmic whisking. *Somatosens. Mot. Res.* 20, 163–169
18 Zucker, E. and Welker, W.I. (1969) Coding of somatic sensory input by vibrissae neurons in the rat's trigeminal ganglion. *Brain Res.* 12, 138–156
19 Szwed, M. *et al.* (2003) Encoding of vibrissal active touch. *Neuron* 40, 621–630
20 Stuttgen, M.C. *et al.* (2006) Two psychophysical channels of whisker deflection in rats align with two neuronal classes of primary afferents. *J. Neurosci.* 26, 7933–7941
21 Szwed, M. *et al.* (2006) Responses of trigeminal ganglion neurons to the radial distance of contact during active vibrissal touch. *J. Neurophysiol.* 95, 791–802
22 Yu, C. *et al.* (2006) Parallel thalamic pathways for whisking and touch signals in the rat. *PLoS Biol.* 4, e124

23 Bermejo, R. *et al.* (2002) Topography of rodent whisking–I. Two-dimensional monitoring of whisker movements. *Somatosens. Mot. Res.* 19, 341–346
24 Shoykhet, M. *et al.* (2003) Protracted development of responses to whisker deflection in rat trigeminal ganglion neurons. *J. Neurophysiol.* 90, 1432–1437
25 Knutsen, P.M. *et al.* (2005) Tracking whisker and head movements in unrestrained behaving rodents. *J. Neurophysiol.* 93, 2294–2301
26 Krupa, D.J. *et al.* (2001) Behavioral properties of the trigeminal somatosensory system in rats performing whisker-dependent tactile discriminations. *J. Neurosci.* 21, 5752–5763
27 Shuler, M.G. *et al.* (2002) Integration of bilateral whisker stimuli in rats: role of the whisker barrel cortices. *Cereb. Cortex* 12, 86–97
28 McKee, S.P. *et al.* (1990) Finding the common bond: stereoacuity and the other hyperacuities. *Vision Res.* 30, 879–891
29 Fee, M.S. *et al.* (1997) Central versus peripheral determinants of patterned spike activity in rat vibrissa cortex during whisking. *J. Neurophysiol.* 78, 1144–1149
30 Derdikman, D. *et al.* (2006) Layer-specific touch-dependent facilitation and depression in the somatosensory cortex during active whisking. *J. Neurosci.* 26, 9538–9547
31 Crochet, S. and Petersen, C.C. (2006) Correlating whisker behavior with membrane potential in barrel cortex of awake mice. *Nat. Neurosci.* 9, 608–610
32 von Heimendahl, M. *et al.* (2007) Neuronal activity in rat barrel cortex underlying texture discrimination. *PLoS Biol.* 5, e305
33 Ritt, J.T. *et al.* (2008) Embodied information processing: vibrissa mechanics and texture features shape micromotions in actively sensing rats. *Neuron* 57, 599–613
34 Wolfe, J. *et al.* (2008) Texture coding in the rat whisker system: slip-stick versus differential resonance. *PLoS Biol.* 6, e215
35 Hentschke, H. *et al.* (2006) Central signals rapidly switch tactile processing in rat barrel cortex during whisker movements. *Cereb. Cortex* 16, 1142–1156
36 Krupa, D.J. *et al.* (2004) Layer-specific somatosensory cortical activation during active tactile discrimination. *Science* 304, 1989–1992
37 Nguyen, Q.T. and Kleinfeld, D. (2005) Positive feedback in a brainstem tactile sensorimotor loop. *Neuron* 45, 447–457
38 Haidarliu, S. and Ahissar, E. (1997) Spatial organization of facial vibrissae and cortical barrels in the guinea pig and golden hamster. *J. Comp. Neurol.* 385, 515–527
39 Haidarliu, S. and Ahissar, E. (2001) Size gradients of barreloids in the rat thalamus. *J. Comp. Neurol.* 429, 372–387
40 Berg, R.W. and Kleinfeld, D. (2003) Rhythmic whisking by rat: retraction as well as protraction of the vibrissae is under active muscular control. *J. Neurophysiol.* 89, 104–117
41 Ferezou, I. *et al.* (2007) Spatiotemporal dynamics of cortical sensorimotor integration in behaving mice. *Neuron* 56, 907–923
42 Ferezou, I. *et al.* (2006) Visualizing the cortical representation of whisker touch: voltage-sensitive dye imaging in freely moving mice. *Neuron* 50, 617–629

Erratum

Cell PRESS

Erratum to "Orthogonal coding of object location" [Trends Neurosci. 32 (2009), 101–109]

Per Magne Knutsen[1,2] and Ehud Ahissar[1]

[1] Department of Neurobiology, Weizmann Institute for Science, Rehovot 76100, Israel
[2] Department of Physics, University of California, San Diego, La Jolla, CA 92093, USA

We apologize for errors within Figures 1, 3 and Box 2 Figure I of the above article, Orthogonal coding of object location, which was published in the February 2009 issue of *Trends in Neurosciences*. In the legend of Figure 1 the word 'straddlers' was incorrectly printed as 'stragglers'; in Figure 3 the four post-stimulus histograms were incorrectly labeled with 'cell' rather than 'cells'; in Box 2 Figure I(b) in the control column the arrow was incorrectly directed upwards, rather than downwards. The correct figures and legends are below.

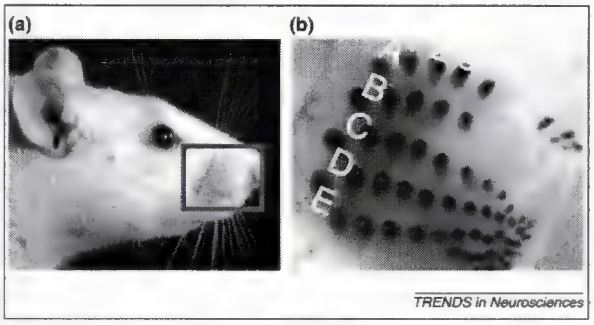


Figure 1. **(a)** The whiskers of the rat mystacial pad (red rectangle) are organized in **(b)** five rows (A–E) and four or more arcs [38]. Four straddlers appear to the left of the letters.

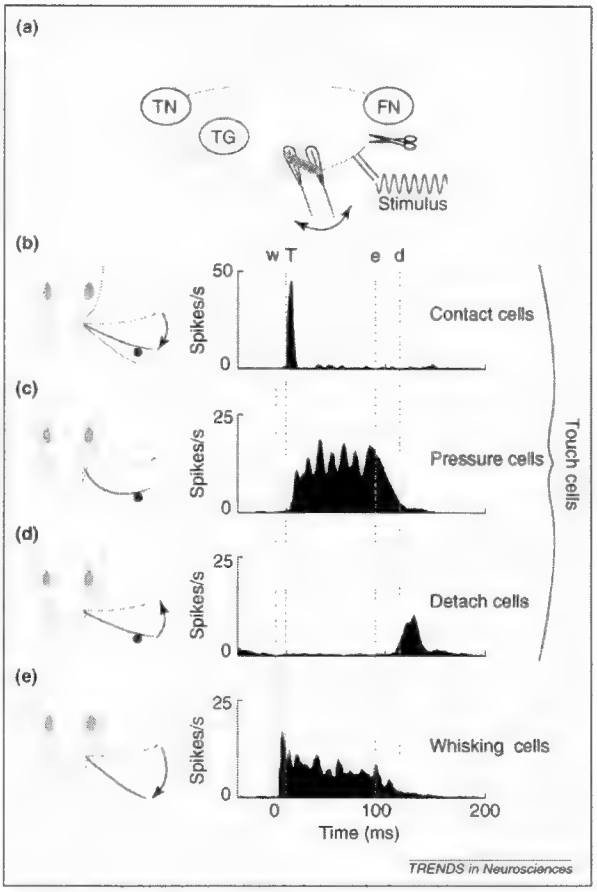


Figure 3. **(a)** Method for artificially inducing whisker movements in the anesthetized rat. Sensory-motor feedback was cancelled by cutting the facial motor (VII) nerve, and whisker movements were controlled by electrically stimulating the distal segment of the nerve [19]. Solid lines indicate known connection and dotted lines indirect connections between trigeminal nuclei (TN) and facial nucleus (FN). During artificial whisking, an object was placed at different locations within the movement path. The most important events in each cycle with the object present (indicated by letters above dashed lines) were onset of movement (w), contact with the object (T), end of stimulation and whisker protraction (denoted with the letter e) and detach of the whisker shaft from the object (denoted with the letter d). TG neurons were grouped into four classes based on response characteristics to these events. **(b)** Contact cells responded only briefly to contact, but not to any other event. **(c)** Pressure cells responded to contact for as long as contact was maintained. **(d)** Detach cells responded only to object detaches. **(e)** Whisking cells responded to whisker movement and were not affected by object contact or detach. The whisking response was present regardless of the presence or absence of the object. Responses of a subpopulation of cells responding to whisker movement were augmented by object contact (whisking/touch cells, not shown). Adapted from Refs [19,21]. Abbreviations: FN, facial nucleus; TG, trigeminal ganglion; TN, trigeminal nuclei.

☆ DOI of original article: 10.1016/j.tins.2008.10.002.
Corresponding author: Ahissar, E. (ehud.ahissar@weizmann.ac.il).

0166-2236/$ – see front matter © 2009 Elsevier Ltd. All rights reserved. doi:10.1016/j.tins.2009.03.001

Box 2. Active versus passive touch

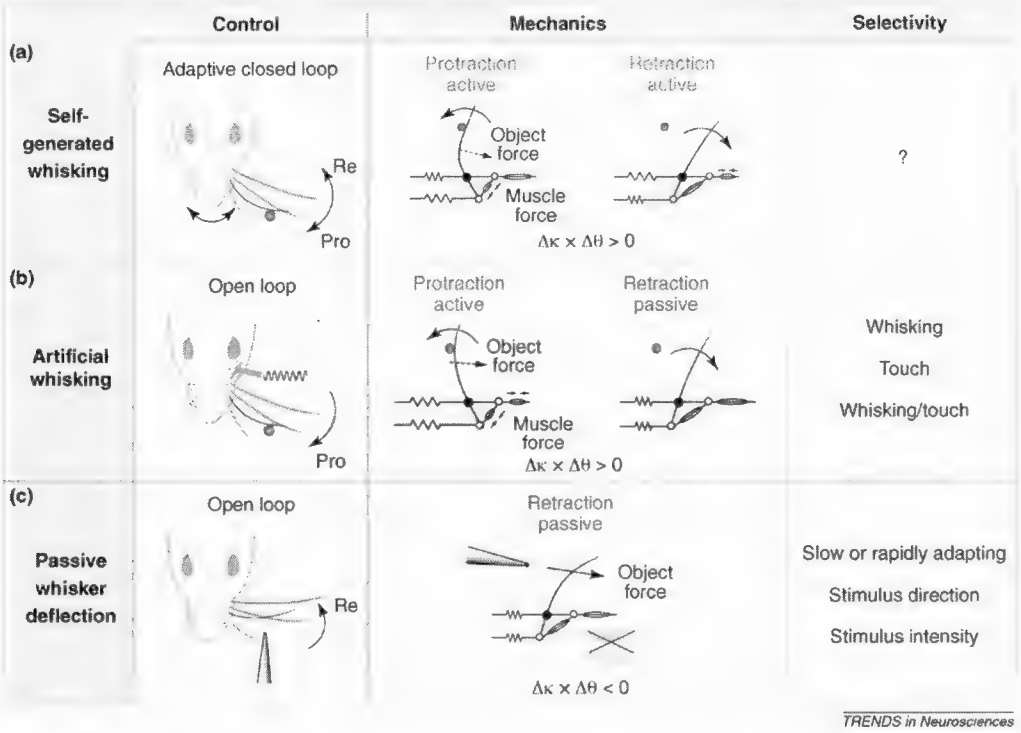


Figure I. Three different paradigms of whisker stimulation and the resulting mechanics and neuronal activity. **(a)** During self-generated whisking, both muscle and contact forces influence whisker mechanics. The neuronal activity of individual primary afferents during such stimulation is unknown (denoted ?). **(b)** Artificial whisking evoked by direct motor-nerve stimulation enables experimental control of active whisking but does not fully reproduce all aspects of normal behavior. Retraction is initiated by cessation of electrical stimulation and is therefore passive, whereas during self-generated whisking dedicated muscles contribute to fast whisker retraction. Neuronal activity during artificial whisking is highly selective to specific events within the whisk cycle, such as contact and motion. **(c)** Passive deflection is the most utilized method of whisker stimulation. During passive deflection, muscle contraction is absent and neuronal selectivity is delineated as a function of adaptation time constants, directional tuning and stimulation intensity thresholds. In the left column, Pro and Re denote protraction and retraction, respectively. In the middle column $\Delta\kappa$ denotes the induced change in whisker curvature and $\Delta\theta$ the induced change in whisker angle.

'Where' and 'what' in the whisker sensorimotor system

Mathew E. Diamond, Moritz von Heimendahl*, Per Magne Knutsen‡, David Kleinfeld§ and Ehud Ahissar‡*

Abstract | In the visual system of primates, different neuronal pathways are specialized for processing information about the spatial coordinates of objects and their identity — that is, 'where' and 'what'. By contrast, rats and other nocturnal animals build up a neuronal representation of 'where' and 'what' by seeking out and palpating objects with their whiskers. We present recent evidence about how the brain constructs a representation of the surrounding world through whisker-mediated sense of touch. While considerable knowledge exists about the representation of the physical properties of stimuli — like texture, shape and position — we know little about how the brain represents their meaning. Future research may elucidate this and show how the transformation of one representation to another is achieved.

Surface texture
Texture relates to the surface pattern of objects. Roughness is one of the attributes of texture. The roughness of an irregular sandpaper-like surface texture is quantified by its grain size; the larger the grains, the coarser the texture.

The classic study by Vincent[1] illustrated that a rat's ability to navigate through a raised labyrinth depends on the use of its whiskers. Whisker touch represents the major channel through which rodents collect information from the nearby environment. They use their whiskers — also called facial vibrissae — to recognize the positions of floors, walls and objects, particularly in dark surroundings. Once they encounter an object they collect additional information about its features, such as its size and shape[2] and surface texture[3–6], through an active process called 'whisking': a sweeping motion of the whiskers forwards and backwards to encounter objects and palpate them[7,8], usually in conjunction with movement of the head[9,10] (see Supplementary information S1 (movie)).

Since neurophysiologists and anatomists began to focus on the rodent whisker system in the 1970's, great strides have been made in unravelling the neuronal pathways that transmit information from the whiskers to the sensory cortex[11–13]. However, the sensory stimuli that were used to probe the system have usually been stereotypical whisker deflections, chosen for their simplicity and ease of presentation. The past few years have seen the initial attempts to understand how the sensory system represents features of the surrounding world that are selected by the animal rather than by the researcher. How is contact with an object transduced into neuronal spike trains? How do these spike trains represent the things that are encountered by the whiskers? This shift in research strategies means that it is critical to summarize what is known and what needs to be better understood. Coding of the direction and frequency of whisker movement has been recently reviewed[12]. Here, we discuss behavioural and electrophysiological studies of tactile discrimination, focusing on how rodents use their whiskers to collect two general types of knowledge about the world: first, the location of objects in the environment, relative to the animal's head ('where'), and second, the properties and identity of objects ('what'). We suggest that 'where' and 'what' can be decoded only through integration of self-generated whisker-motion signals. Finally, we indicate future directions of research that seem likely to be productive.

Organization of the whisker sensory system

The structure that anchors a whisker to the skin is called follicle. It gives tactile sensitivity and motion to the whisker, which is itself inert material. Each follicle is innervated by the peripheral branches of about 200 cells of the trigeminal ganglion[14], whose nerve endings convert mechanical energy into action potentials (FIG. 1a). These afferent signals travel past the cell bodies in the trigeminal ganglion and continue along the central branch to form synapses in the trigeminal nuclei of the brainstem[15,16]. The trigeminal nuclei convey afferent vibrissal information to the thalamus via parallel pathways (BOX 1) that then continue to the barrel field of the somatosensory cortex[17].

The large whiskers on each side of a rat's snout (also called macrovibrissae) are arranged in a grid made up of 5 rows, designated A to E, and several numbered arcs, so that an individual whisker can be identified by its row

*Cognitive Neuroscience Sector, International School for Advanced Studies (SISSA), 34014 Trieste, Italy; Italian Institute of Technology — SISSA unit.
‡Department of Neurobiology, Weizmann Institute of Science, Rehovot 76100, Israel.
§Department of Physics, University of California, San Diego, La Jolla, California 92093, USA.
Correspondence to M.E.D.
e-mail: diamond@sissa.it
doi:10.1038/nrn2411

© 2008 Macmillan Publishers Limited. All rights reserved.

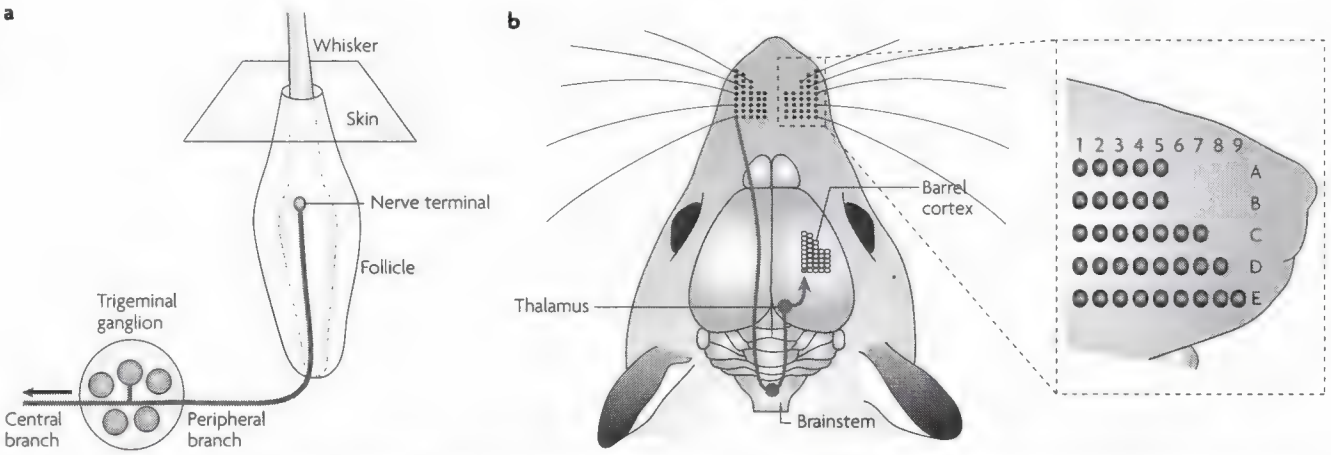


Figure 1 | **Layout of the whisker sensory pathway. a** | In each whisker follicle, mechanoreceptors respond specifically to rotation of the follicle by its muscles or to deflection of the whisker shaft by external contacts, both of which encode information about the direction, velocity and duration of displacements and torques. **a** | Schematic illustration of a mechanoreceptor terminal. Afferent sensory fibres travel together in the infra-orbital branch of the trigeminal nerve to the cell bodies, which are located in the trigeminal ganglion that lies just outside the brainstem. The central branch of the ganglion cell projects toward the trigeminal complex in the thalamus (arrow). **b** | The vibrissae form a two-dimensional grid of five rows on each side of the snout, each row containing five to nine whiskers ranging between 15 and 50 mm in length (see inset). After a synapse in the brainstem, axons of the second-order neurons cross the midline and travel to the thalamic somatosensory nuclei; thalamic neurons project to the barrels in the primary somatosensory cortex.

and arc coordinates (for example, C3). This whisker array is identical in all rats (FIG. 1b). The layout of the barrels in the somatosensory cortex replicates the layout of the whiskers on the snout[18]. The clear anatomical maps at each level of the ascending pathway have long suggested a 'whisker-to-barrel' connection. Even though neurons in the barrel cortex possess a receptive field that extends to several whiskers, it is usually clear — both in anaesthetized and in awake animals — that a single, topographically appropriate whisker exercises the strongest influence on a neuron's firing (reviewed in REFS 12,19).

'Where' in the whisker sensory system

Many nocturnal animals (and some diurnal ones), including numerous rodent and insectivore species, use their whiskers to detect the presence and location of objects when moving through an environment. For example, in the dark, rats can learn to 'gap-cross', that is, to perch at the edge of a raised platform and use their whiskers to localize a second platform before crossing the gap to retrieve a reward on the second platform[20,21]. In a similar test, when rats are placed on a platform that is elevated above a glass floor, they whisk against the glass surface before stepping down; they use visual information to detect the floor only if their whiskers are cut[22]. Studies of how rats use their whiskers to determine the configuration of objects in the environment are summarized in the next section.

Behavioural measures of object localization. The position of an object in head-centered coordinates (that is, relative to an animal's head) can be defined along three axes: the medio-lateral (radial) axis, the rostro-caudal (horizontal) axis and the dorso-ventral (vertical) axis. A number of behavioural studies have established that rats use their whiskers to perceive space in each of these dimensions.

The ability to determine object location in the radial dimension was tested in experiments in which rats had to classify the width of an alleyway as either 'wide' or 'narrow' (REF. 23). The rats were trained to align their head between two equidistant walls and to palpate them using only their macrovibrissae. By gradually decreasing the difference between 'wide' and 'narrow' across training sessions, rats learned to distinguish between aperture widths that varied by as little as 3 mm. Active whisking was not observed during the behaviour, and paralysis of the whisker pad by bilateral transections of the facial nerves did not reduce the success rates. Instead of whisking, rats brought their whiskers into contact with the alleyway walls through a combination of head and body movements. Although each whisker encodes radial distance independently, multiple whiskers appear to act together: removal of increasing numbers of whiskers resulted in a progressive impairment of performance until chance performance was reached when only a single whisker was left intact on either side of the snout. These results show that rats integrate signals about contact from many whiskers to obtain accurate readings of radial distance.

A follow-up study[24] showed that rats were capable of comparing the relative bilateral radial offset between the alleyway walls by successfully discriminating the walls as either 'equidistant' or 'non-equidistant'. Again, in this task the rats did not show any active whisking while palpating the walls. The difference between near and far, on each side, was 11 mm.

A behavioural paradigm (FIG. 2) was recently developed to study object localization in the horizontal dimension[25]. A vertical pole was placed on each side of the rats' snout at different horizontal positions, with the posterior pole in a fixed reference location. The rats had to detect whether

Macrovibrissae
Long (3–40 mm), sparsely spaced (2 per cm^2) whiskers located on the middle and posterior part of a rat's snout. They are ordered in a regular, geometric grid and exhibit prominent forward and backward whisking motion

Barrel
A set of neurons in the somatosensory cortex. Each barrel is responsible for processing the input from one whisker

© 2008 Macmillan Publishers Limited. All rights reserved.

the left or the right pole was at the horizontal reference location, and then orient towards a liquid-dispensing spout on that side. Through successive stages of training, rats learned to position their snout against a central nose-poke, so that only the macrovibrissae were in contact with the poles. Most rats were able to discriminate the location of the reference pole even when the horizontal offset of the distractor pole was as small as 1.5 mm, or

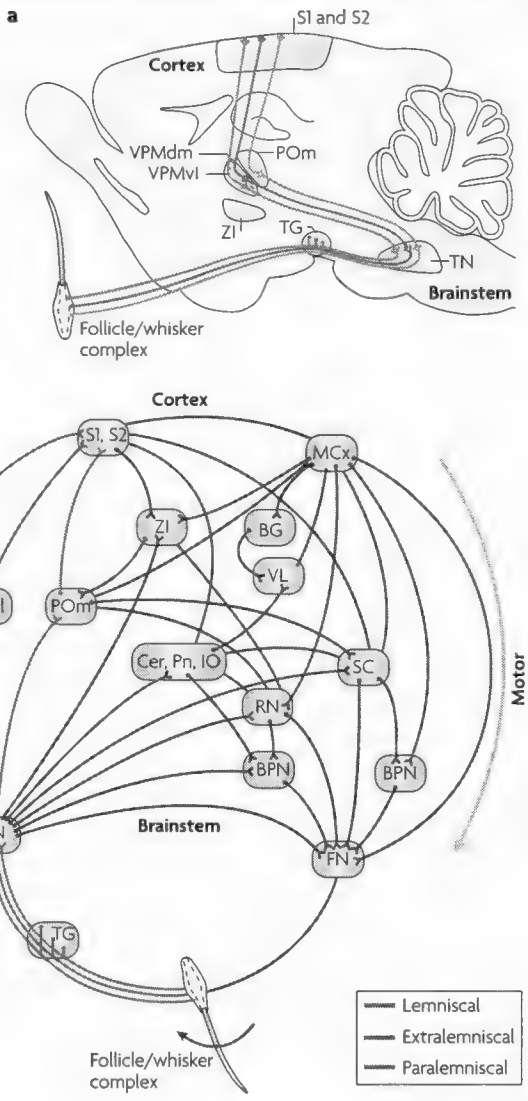
Box 1 | **Parallel pathways to the cortex**

Neurons of the trigeminal ganglion (TG) send a peripheral branch to the skin and a central branch into the trigeminal nuclei (TN) of the brainstem. Afferent signals travel past the cell bodies in the TG and continue along the central branch to form synapses in the TN. Multiple afferent pathways originate from these nuclei, some of them forming sensorimotor loops below the cortical level[11]. Three afferent pathways eventually reach cortical levels (see panel **a**).

Lemniscal pathway (red). Neurons in the principal TN are clustered into 'barrelettes'. The axons of these second-order neurons cross the midline and travel, via the lemniscal pathway, to the 'barreloids' of the dorsomedial section of the ventral posterior medial nucleus (VPMdm) of the thalamus. Both barrelettes and barreloids are sets of modules arranged as a topographic projection of the whiskers themselves; neurons in a given module respond principally to the somatotopically connected whisker.
The axons of VPMdm neurons project to the primary somatosensory cortex (S1), where they terminate in 'barrels', dense clusters of small neurons in layer IV[18,66,67].

Extralemniscal pathway (blue). Neurons in the caudal part of the interpolar TN are also clustered into whisker-related barrelettes. They project to the ventrolateral domain of the VPM (VPMvl), where neurons are clustered into the 'tails' of the VPMdm barreloids[68,69]. The axons of VPMvl neurons project to the septa between the barrels of S1 and to the secondary somatosensory cortex (S2)[68].

Paralemniscal pathway (green). Neurons in the rostral part of the interpolar TN are not spatially clustered. They project, among other targets, to the medial sector of the posterior nucleus (POm)[68,69] and to the zona incerta (ZI)[70]. The axons of POm neurons project to targets immediately ventral to the barrels, in layer 5a of S1 (REFS 71–73), S2 (REFS 68,74,75) and to the primary motor cortex (MCx)[76]. Contrary to the lemniscal pathway, the paralemniscal pathway is not spatially-specific and seems to integrate multiple-whisker information[77,78].



Recently, a fourth pathway, ascending from the principal TN through the 'heads' of the barreloids in the VPMdm, has been reported[79]. The cortical targets of this pathway have not yet been determined.

The functions of the different pathways have not yet been directly tested and hypotheses vary across research groups. In our view, the response selectivity during artificial whisking suggest that paralemniscal neurons in the POm convey information about whisking kinematics, extralemniscal neurons in the VPMvl convey contact timing, and lemniscal neurons in the VPMdm convey detailed whisking and touch information[78,80–82].

The pathways are part of a complex network of sensorimotor vibrissal loops (panel **b**), which ascend through the pathways discussed above and then descend back to the whiskers through motor pathways (not discussed in this Review).

Additional abbreviations: BG, basal ganglia; BPN, brainstem premotor nuclei (arbitrarily divided to two oval circles); Cer, cerebellum; FN, facial nucleus; IO, inferior olive; Pn, pontine nuclei; RN, red nucleus; SC, superior colliculus; VL, ventrolateral thalamic nucleus. Connections indicated by lines without a synapse-like ending are reciprocal.

© 2008 Macmillan Publishers Limited. All rights reserved.

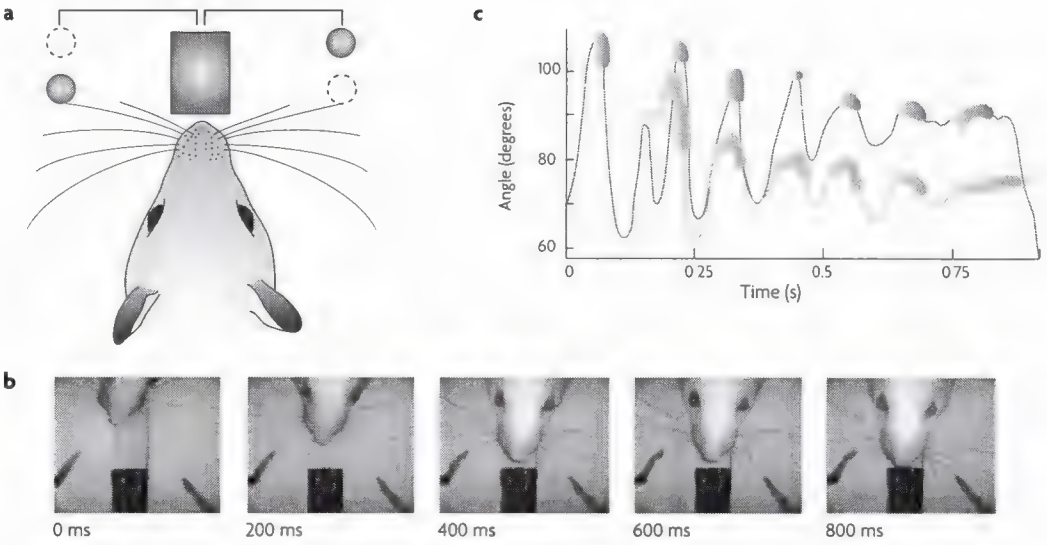


Figure 2 | **Bilateral comparison of horizontal object localization. a** | Rats were trained to align their head with a nose-poke. Vertical rods were placed on both sides of the head (circles) and the rats discriminated their relative rostro-caudal positions. Grey circles indicate the position of the rods in trials in which the left rod is placed posterior to the right rod. Dashed circles indicate the position of the rods in trials in which the right rod is placed posterior to the left rod. **b** | Typical head and whisker movements during a horizontal object-localization task. Under infrared light (in which rats cannot see), the rat aligns its head to the nose-poke and uses its whiskers to contact and determine the relative horizontal locations of the two vertical poles. **c** | Whisker movements during one trial. The rat entered the discrimination area at time 0 and exited after about 1 sec. During this period, it swept its whiskers back and forth in a rhythmic manner to contact the poles. The red line indicates the angle of the right C2 whisker and the blue line indicates the angle of the left C2 whisker. Contact between whisker and object is indicated by the thicker areas on the lines. Figure modified, with permission, from REF. 25 © 2006 Society for Neuroscience.

6° of whisker sweep. Some rats performed well when the difference between the reference and distractor poles was only 0.24 mm, or 1°. Sensorimotor function in this task differed from that in the radial object-localization task in two ways. First, sensing horizontal spatial offsets required whisking: rats actively moved their whiskers back and forth 3–6 times per trial (with a trial lasting approximately 500 msec). When whisking motion was abolished by bilateral transection of the motor nerves, performance accuracy dropped to chance level. Second, partial whisker removal did not impair accuracy; rats performed equally well, or better, with just a single, intact left and right whisker. Interestingly, although rats were allowed to move their head and body, better performance in the horizontal object-localization task was correlated with fewer (and smaller) head-movements, suggesting that head-stabilization is part of the sensory-motor horizontal localization strategy.

The above tasks involve comparing the positions of two objects relative to each other. Other whisker-dependent tasks require the rat to know the position of an object relative to the animal itself. When a rat measures the location of a platform across a gap using a single whisker[20,26], it probably does so by sensing the whisker-object contact point in head-centred coordinates. This capacity was investigated in psychophysical experiments in which rats had to detect, with a single whisker, the angular position of one pole relative to their face (FIG. 3). The rats performed this task with an angular resolution equal to or better than 15° (REF. 27). Because the rats were trained to suppress head-movements, the only way that they could contact the object was through whisker movements. Thus, for both types of horizontal localization task — comparing the relative locations of two objects and finding the absolute location of an object in space, respectively — the animal uses reference signals about vibrissa position[28,29]. Further work is required to understand the nature of such reference signals and how they are exploited in different tasks.

Independently of the nature of the reference signal, it is clear that for relative sensing (FIG. 2; also see REF. 30) active-touch produces hyperacuity. Hyperacuity can also be found in vision[31]: when comparing the locations of two concurrently present objects, acuity reaches ~1° with vibrissal touch and ~3 arcseconds with human vision. These levels of acuity are well beyond the spatial resolution of the receptors (whisker follicles and photoreceptors) themselves. By contrast, when localizing objects in body or head-centred frameworks (FIG. 3), acuity is lower (less than 15° with vibrissal localization, ~1° with human vision).

Neuronal encoding of object location. What signals do neurons along the trigeminal pathway carry about object position? Although it is important that this question be investigated in awake behaving animals, a good starting point is to measure the activity of sensory receptor neurons during whisker motion that is induced artificially by electrical stimulation of the facial motor nerve in anaesthetized animals[29,32]. In such experiments,

Hyperacuity
Sensory acuity that exceeds the spatial resolution of the sensor. Vibrissal hyperacuity is the ability to resolve spatial offsets that are smaller than the inter-vibrissal spacing.

Sensory receptor neuron
Neuron that converts a physical stimulus into electric impulses. In the whisker system, the cells of the trigeminal ganglion act as sensory receptor neurons

© 2008 Macmillan Publishers Limited. All rights reserved.

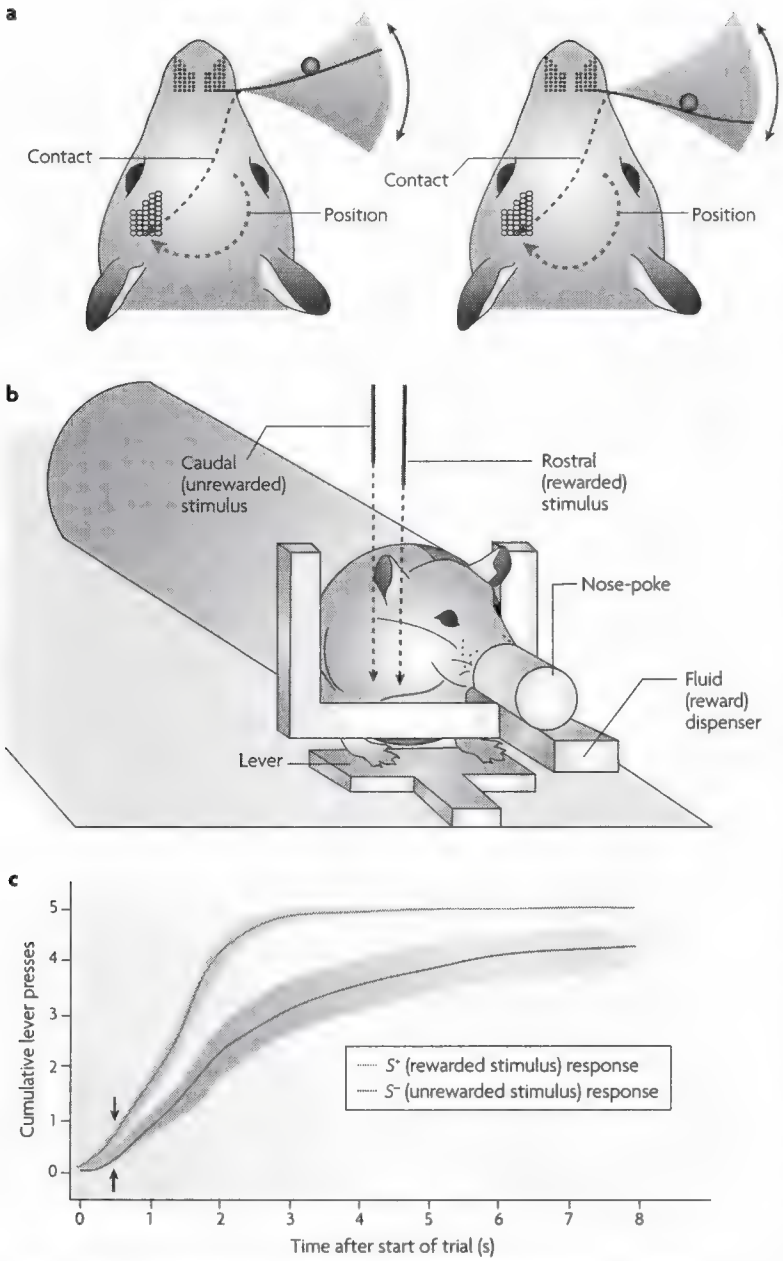


Figure 3 | **Absolute horizontal object localization. a** | The absolute localization of a vertical rod (filled grey circle) requires the confluence of a contact signal (black dashed line) with a signal related to self-generated whisking, shown here schematically as a graded-colour fan. In the left panel, the whisking signal (indicated by the grey dashed arrow pointing to the contralateral barrel cortex) conveys that the whisker is in the anterior position at the instant of object contact. In the right panel, the whisking signal (red dashed arrow) conveys that the whisker is in the posterior position at the instant of object contact. **b** | Apparatus for testing of absolute horizontal object localization. Trials start when an animal interrupts the nose-poke sensor, causing either the rostral or caudal rod to descend into the vibrissa field. The stimuli are positioned through a circular guide that is fixed relative to the nose-poke. Lever presses in response to the S^+ stimulus, either rostral or caudal for a given animal, were rewarded with a drop of water in the fluid dispenser. **c** | Temporal profile of cumulative lever press counts for one session, averaged separately over S^+ (green line) and S^- (red line) trials. Differences in the counts of lever pressing indicate that the animal recognized the position of the rod. The curves give the mean ± 2 SEM cumulative lever press counts for S^+ trials (green) and S^- trials (red). The arrows at 0.5 s mark the time point after which curves are non-overlapping. Figure modified from REF. 27.

neuronal responses have been measured during two conditions, namely when the whisker moved in the air without touching anything and with a vertical pole (extending the entire height of the whisker array) positioned at different locations in the path of the moving whiskers. In these conditions, three functional classes of primary sensory neuron were detected: first, 'whisking cells', which fired during whisking *per se*, regardless of whether the whiskers touched anything; second, 'touch cells', which fired upon contact, sustained pressure or detachment, but not to whisking alone; and third, 'whisking/touch cells', which fired during both types of event.

The nature of afferent signals in the awake rat is less clear. By recording neuronal activity in the trigeminal ganglion of freely moving rats and comparing epochs of massive vibrissal touch (which caused gross bending of whiskers to less than half of their length) to epochs without touch, a wide distribution of selectivity was noted, from neurons that responded mostly to whisking to those that responded mostly to touch[33]. Whether a stronger selectivity exists in the awake rat among individual afferents and during epochs of light touch is not yet known.

However, assuming that the neuronal responses to whisking and touch that are observed during artificial whisking can be verified in awake animals, object position could be encoded as follows: radial location could be encoded by firing rate and/or by spike count. As a whisker sweeps forward, object contact would be reported by touch cells and whisking/touch cells. The majority of these cells show an increase in firing rate as the radial distance of the object from the whisker base decreases[32]. This could result from the progressively greater force applied to receptors in the whisker follicle as the radial distance between object and whisker decreases[34], because less energy goes into bending the whiskers when the thicker, proximal part of the whisker shaft contacts the object.

Horizontal location could be encoded through the same contact signal, but by spike timing rather than spike count. As a whisker contacts an object progressively later in a whisk cycle the farther the object is positioned forward, the onset time of the contact signal correlates with the horizontal coordinate. However, this form of temporal code can only be decoded if there is a reference signal that encodes the spatial location of the whisker over time (FIGS 2,3). In that case, the reference signal can be compared with the contact signal to extract object position[29,35]. The spiking activity of whisking cells located in the trigeminal ganglion[29] could provide such a reference signal, as these cells transmit information about the angular phase and position of the whiskers. Experiments in awake behaving rats have shown that this whisking signal is conserved all the way to the barrel cortex[28]. So, neurons that receive both phase-specific whisking signals and touch signals could decode horizontal object position by detecting the concurrence of the two types of signal. From studies in anaesthetized rats, it is known that whisking signals and touch signals are still separate at the level of the

© 2008 Macmillan Publishers Limited. All rights reserved.

thalamus[36]. In the barrel cortex, whisking and touch separation is less distinct[37], although cortical activity has been shown to be modulated by whisking and touch at both the single-cell[6,28,37–40] and population levels[41–43]. Recent findings suggest that whisking and touch signals converge on single cortical neurons whose firing reports the horizontal coordinate of a touched object relative to the face (discussed in REF. 44). Their output depends on a nonlinear interaction between whisking and touch signals: whisking strongly modulates the response of these neurons to touch, possibly through shunting inhibition or a functionally equivalent gating mechanism.

Encoding of vertical location has not yet been examined in combined physiological–behavioural studies, but a simple and plausible hypothesis can be formulated. Because the whisk trajectory of a single whisker is coplanar with a whole row of whiskers, vertical location could be based on an 'identity code': the mere presence of a touch response in a neuron that is related to a specific whisker, located anywhere along the trigeminal pathway, could report contact with an object at the elevation of that whisker.

An interesting feature of the proposed encoding schemes is that they can coexist in the activity pattern of the primary sensory neurons. The way in which rats use their whiskers is consistent with this suggestion. For example, when determining an object's horizontal location, rats actively whisk and their performance accuracy correlates with the energy put into whisking; whisking paralysis induced by motor nerve lesion annuls performance and rats continue to perform the task at high accuracy with only a single intact whisker on each side[25,27]. These behavioural findings suggest that the encoding of horizontal location depends on kinetic information that is fully available from individual whiskers. This is in agreement with a coding scheme that involves temporal comparison between a touch signal and a reference whisking signal; the same data argue against either spatial-coding or rate-coding schemes. By contrast, when determining an object's radial location, rats suppress whisking; whisking paralysis does not impair performance and accuracy depends on the number of intact whiskers[23]. These observations indicate that radial location encoding is independent of whisking-related signals but seems to be based on contact-evoked firing rates of primary sensory touch neurons. The single-cell strength of the signal for radial location is weak, with just a subset of cells reliably reporting radial location differences equivalent to 30% of the whisker length[32]. This low encoding resolution explains why rats require large numbers of whiskers: the overall signal strength can be improved by pooling the signals from multiple touch cells that are associated with the set of contacting whiskers.

Thus, single-cell recordings in anaesthetized rats and psychometric and motor constraints observed in behaving rats are consistent with a space–time–rate triple-coding encoding scheme of object location. Demonstrating the operation of this encoding scheme in awake, behaving rats at the neuronal level remains a challenge.

Temporal code
A coding scheme where not only the rate of action potentials is informative, but also their firing pattern. Two stimuli which evoke the same firing rate may be discriminated if they evoke unique firing patterns.

Spatial-coding
A coding scheme where the position of the active neuron carries critical information. For example, if C3 neurons fire, the stimulus location is specified as being in the trajectory of the C3 whisker. This type of coding is sometimes called 'identity coding'.

Rate-coding
A coding scheme where a stimulus' quality, such as its intensity, is transmitted by the quantity of spikes emitted per unit of time.

Microvibrissae
Short (few mm), densely spaced (87 per cm^2) whiskers located on the anterior part of a rat's snout. They are not ordered in a regular grid and exhibit little or no whisking motion

'What' in the whisker sensory system

It is natural for whisking animals to make behavioural choices according to the identity of the objects palpated by their whiskers. For example, under laboratory conditions, when rats are faced with two platforms, each covered with a different texture, they can easily learn to identify the reward-associated texture and jump onto the correct platform[3–6]. In tasks such as this, the high accuracy of the rats' judgments, combined with the short amount of time between first whisker contact with the platforms and the onset of the behavioural action (as little as 100 ms), indicates that whisker-mediated object identification is enormously efficient; as such, the neuronal mechanisms underlying this capacity can provide crucial knowledge to neuroscientists investigating other sensory modalities and to the field of biomimetics, which aims to develop biologically-inspired artificial tactile systems.

Judgment of shape. Shape is an important clue about the identity of an object. In an experiment that set out to determine whether the whisker sensory system can support shape discrimination, rats were trained in the dark to judge the shape of small (less than 1 cm) cookies that were distributed on a table in front of them[2]. All but one of the cookies possessed the same shape and contained caffeine, a bitter but odourless substance that is aversive to rats. One cookie had a different shape and did not contain caffeine and was therefore edible. Rats learned to identify the untainted cookie by quickly palpating each cookie with the small whiskers around the nose and mouth (the so-called microvibrissae). At the time of this groundbreaking study, high-speed video was not available to document whisking, but whisking as a means of reconstructing shape has been documented more recently by observation of the Etruscan shrew (FIG. 4a) through high-speed video in the dark[45]. This animal, the smallest terrestrial mammal, identifies prey (crickets) and selects its bite location possibly after a single whisk on the potential target. Shape cues, such as the cricket's legs, guide the behaviour (FIG. 4b,c).

It is likely that rats use their longer and more widely spaced posterior whiskers (macrovibrissae) to judge the form of objects that are too large to be spanned by the grid of microvibrissae. Though there are as yet no observations of whisker dynamics during shape judgement, it was recently proposed that whiskers have a role in this process. The hypothesis was based on data obtained from an artificial whisker apparatus[34] in which the bending of a whisker-like fibre varied as it was swept along a surface — the fibre straightened slightly when it extended into cavities and curved as it passed over protuberances. The torque acting on the fibre was read off from a strain gauge at the base of the fibre and, after many sweeps, a good approximation of shape features could be reconstructed. Because it is likely that the whisker follicle contains sensory receptors to encode torque, the analogous strategy could be the starting point for shape recognition.

© 2008 Macmillan Publishers Limited. All rights reserved.

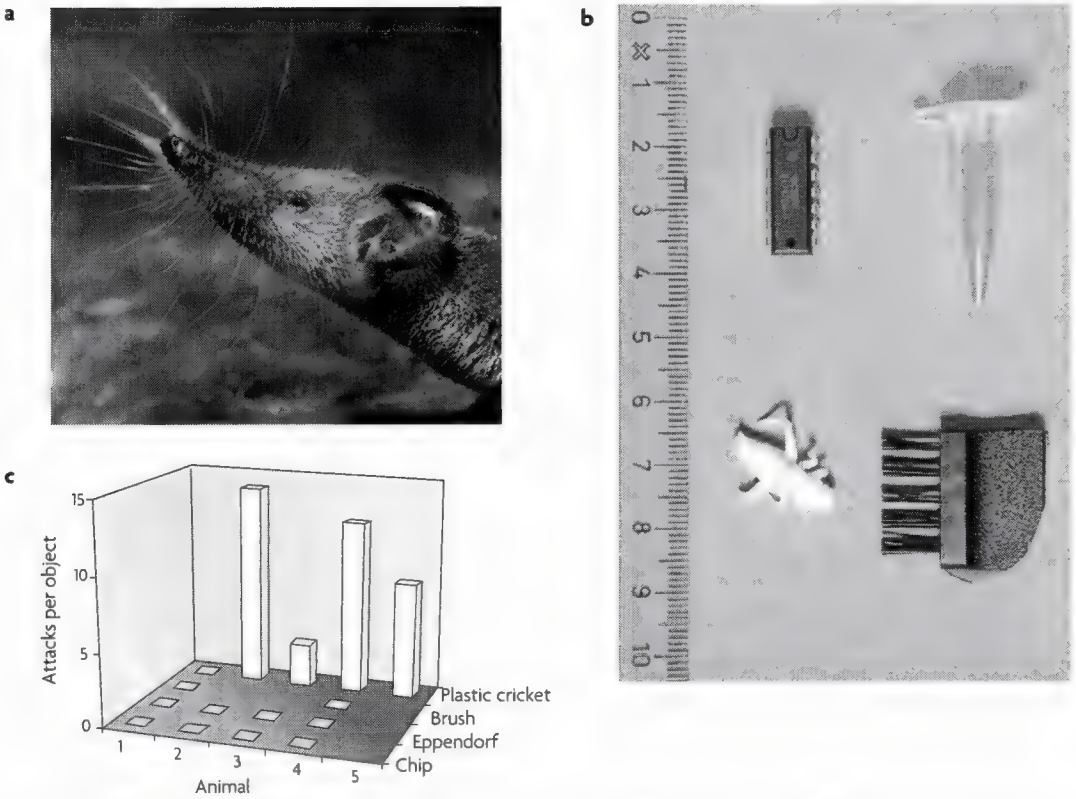


Figure 4 | **Object recognition by shape. a** | Whisker-laden snout of the Etruscan shrew. **b** | Objects placed in an arena near a hungry shrew. The arena was lit only with infrared light, in which the animal cannot see. One object was shaped like a cricket, the preferred prey of the shrew. **c** | Shrews attacked plastic crickets, but not other objects, after palpating them with their whiskers, indicating that shape is both necessary and sufficient to trigger an attack. Animal number 1 failed to attack the plastic cricket, which had lost some of its shape cues in previous encounters; the same animal did, however, attack newly made plastic crickets in a later stage (data not shown). Panel **a** © Dietmar Nill/linea images. Panel **b** and **c** were modified, with permission, from REF. 45 © (2006) National Academy of Sciences.

Judgement of texture. Texture is another physical property that can be a reliable clue about the identity of an object. For example, the walls and floors that rodents contact as they navigate, and the materials they use in nest building[46], are all characterized by small-scale surface features. One way to test texture discrimination is to train an animal to associate each of two textures with a specific action[3,4]. This approach has shown that rats can learn to associate one of the textures with a reward and by whisker palpation can reliably discriminate a smooth surface from a rough surface containing shallow (30 μm) grooves that are spaced at 90 μm intervals[3]. It has been proposed that the capacity of the rodent whisker system to distinguish texture is comparable to that of fingertips in primates[47,48], though direct comparisons do not yet exist.

In a recent study[6], rats were trained to perch at the edge of an elevated platform, extending their whiskers across a gap to touch a textured plate mounted on a second platform. In each trial, the rat had to identify the texture — either smooth or rough — and then withdraw and turn to a water spout to receive a reward. The texture indicated whether the reward would be presented to the left or right of the rat (FIG. 5a). As the rat probed the texture, whisker motion was filmed with high-speed cameras (FIG. 5b). Texture identification was efficient and accurate. On a typical trial, an individual whisker made 1–3 touches of 24–62 ms duration each before the rat made its choice, summating to a total touch-time per whisker of 88–224 ms; the time from first whisker contact to the choice action was 98–330 ms (interquartile ranges). None of these contact parameters differed according to the texture presented to the animals, suggesting that motor output was not modulated by the contacted texture.

Neuronal encoding of texture. Although the barrel cortex is known to be essential for the discrimination of texture[4], the neuronal representation of texture has been difficult to uncover[5]. A first clue came from experiments in which the whiskers of anaesthetized rats were made to move by electrical stimulation of the motor fibres that innervate the whisker muscles[49]. Movement of a whisker across a given texture gave rise to a vibration at the whisker base with a kinetic signature that was characteristic of the contacted surface and that was defined by the temporal profile and temporal integral of whisker velocity[49,50]. With these texture-induced vibrations

Kinetic signature
The temporal profile of a whisker's movement as it slides across a texture. It is characteristic of the texture, modulated by sliding speed and whisker length (among other factors), and appears to be quite robust.

© 2008 Macmillan Publishers Limited. All rights reserved.

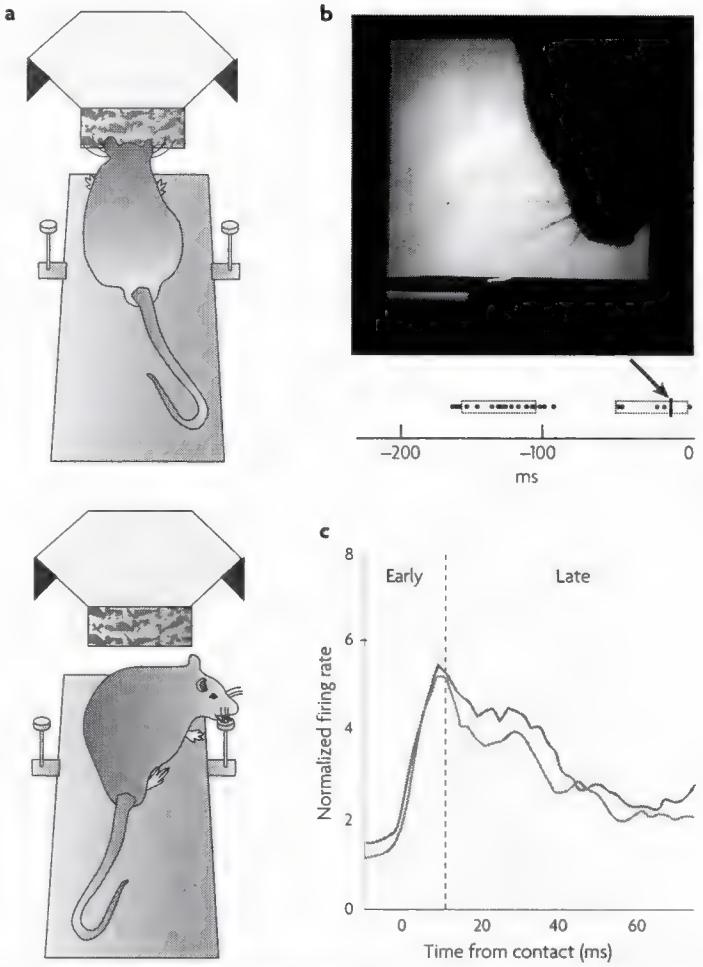


Figure 5 | **Texture discrimination task. a** | Upper panel: the rat extends to touch the texture (textured rectangle) with its whiskers. Lower panel: having identified the texture, the rat turns to the drinking spout on the right to receive a water reward. **b** | Captured by a high-speed camera under infrared light, the rat touches the textured plate with whisker C2 (yellow). Below the film frame, the spike train recorded from barrel C2 on this trial is shown. The red boxes indicate the touch times and the arrow points to the time at which the image was captured. 0 ms is the moment the rat withdrew from the plate. **c** | Dynamics of the neuronal response during whisker contact. Whisker contacts with the textured plates were documented from high-speed films simultaneously with recordings of neuronal activity in the barrel cortex. The instant of whisker contact was set at 0 ms. For both textures, the firing rate increased rapidly immediately after contact (4–11 ms, 'early'). Subsequently ('late'), the response patterns separated according to texture: a significantly higher firing rate was found for rough (red) compared with smooth (blue) textures. Figure modified from REF. 6.

presented as stimuli, the responses of sensory receptors and neurons in the whisker area of the cortex were recorded. This uncovered two potential coding mechanisms by which texture might be represented: textures with similar overall coarseness were discriminable by distinctive, temporally precise firing patterns, whereas textures of significantly different coarseness were distinguished by firing rate — rough textures evoked more spikes than smooth textures[51].

In awake, freely behaving rats, stimuli are generated by the animal through its own whisker motor programme. To test whether the results from the studies in anaesthetized rats described above are applicable to awake behaving rats, animals were trained to perform texture discriminations while neuronal activity (single- or multi-units) in the barrel cortex was measured[6]. The specific aim of this experiment was to verify the prediction that roughness was encoded by the firing rate of barrel cortex neurons[49]. Based on the well-known connection between one cortical barrel and its topographically matched whisker (reviewed in REF. 12), spikes could be aligned to the moment of contact of the principal whisker with a textured surface, as judged from high-speed films (FIG. 5b). The responses were then divided into two separate traces that corresponded to whisker contacts with rough and smooth textures, respectively (red and blue trace in FIG. 5c); during the initial, sharply rising response phase (4–11 ms, marked 'early' in FIG. 5c), there were no significant texture-related differences in neuronal firing. However, in the second phase, neurons showed a greater firing rate in response to their whiskers' touching rough surfaces (red trace) compared with smooth ones (blue trace). This result suggests that the firing rate might be the fundamental coding mechanism for texture. However, this conclusion rests on the assumption that a rat can decode neuronal activity in precise temporal alignment with individual whisker contacts. Thus, in a second analysis no precise knowledge of whisker contact times was assumed: neuronal activity was measured before the rat made a behavioural choice, that is, before the moment when it stopped examining the texture. Neuronal activity during the last 75 ms before the animal made a choice transmitted the most informative signal; in this window, neuronal clusters carried, on average, 0.02 bits of information about the stimulus.

Analysis of trial-to-trial variability of the posited neuronal coding feature is a powerful approach for learning how cortical activity guides behaviour[52]. In the texture discrimination task, an examination of the neuronal responses in trials in which the rat misidentified the texture revealed that, in contrast to correct trials, neuronal firing rates were higher in response to contact with smooth rather than rough textures. An analysis of high-speed films suggested that in incorrect trials the inappropriate signal was due, at least in part, to non-optimal whisker contact. These experiments clearly point to the firing rate of barrel-cortex neurons in each trial as the critical neuronal feature underlying the animal's judgement of texture. However, the features of whisker motion that encode texture during active stimulus discrimination are currently subject of debate[53–55].

Sensorimotor integration

In the sense of touch, it is the motion of the sensory receptors themselves that leads to an afferent signal — whether these receptors are in our fingertips sliding along a surface[56] or in a rat's whisker follicles as it palpates an object. Thus, tactile exploration entails the interplay between motor output and sensory input. Just as we would not be able to estimate the weight of an object we are lifting without taking into account the motor signals that produce muscle contraction, the afferent signal from a whisker cannot be optimally decoded without

Principal whisker
The whisker that upon stimulation evokes the strongest response in a given sensory neuron.

© 2008 Macmillan Publishers Limited. All rights reserved.

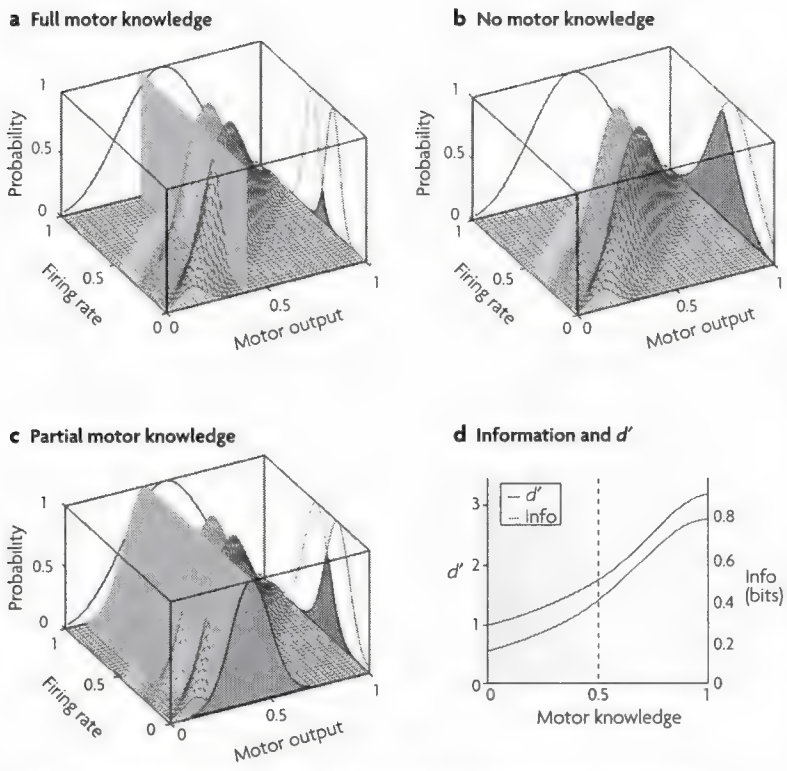


Figure 6 | **The role of motor signals in decoding sensory inputs.** Illustration of a model of active sensorimotor integration for an animal that has to discriminate between two objects according to the size of the neuronal response that is evoked by whisker contact with the objects. The model assumes, first, that the greater the difference in spike counts that are associated with two stimuli, the more reliable the resulting discrimination; and, second, that for contact with a given object, a stronger motor output leads to a higher firing rate. In panels **a**–**c**, the z-axis depicts the probability distributions for firing rate (x-axis) and motor output (y-axis) for rough (red) and smooth (blue) textures. **a** | For a precisely known motor output (vertical slice), the firing-rate distributions are given by the conditional distributions, which are projected on the right wall of the graph. **b** | If the motor output is unknown, the firing rate is distributed following the marginal distributions, shown on the right wall. Note the much greater variance and overlap. **c** | If the motor output is known with some Gaussian uncertainty, the firing rate is distributed following a weighted average of conditional distributions, visualized here by an intersection with a Gaussian distribution. The resulting firing-rate distributions, projected on the right wall, have an intermediate degree of overlap. **d** | d' and information (Info) of firing rate about texture is shown as a function of motor knowledge. A value of 0 corresponds to no motor knowledge (as in part **b**), 1 is full knowledge (as in part **a**) and 0.5 corresponds to the level of partial knowledge (shown in part **c**).

information about the movement that generated the tactile signal to begin with. In the whisker sensorimotor system, the perturbation of the whisker movements that result from contact with an object gives rise to sensory signals that carry information about the object. In earlier sections, we reviewed evidence that rats localize objects by combining contact-evoked afferent signals with self-generated motion signals. Here, we present a simple model of active sensorimotor integration where the animal must discriminate between two objects according to the size of the neuronal responses that are evoked by whisker contact with the objects. It is based on two biologically plausible assumptions. First, the greater the difference in spike counts that are associated with two stimuli, the more reliable the resulting discrimination. Second, for contact with a given object, a stronger motor output (where strength refers to a combination of motor variables — for example, the amplitude and speed of a whisk) leads to a higher firing rate.

To examine the role of self-induced motion in object coding, we will consider the discrimination of surface texture (FIG. 6). According to evidence presented in the section on neuronal encoding of texture (FIG. 5), contact with a rough surface produces, on average, a higher firing rate than contact with a smooth surface. Accordingly, in FIG. 6 the two textures are associated with the high-firing rate distribution (red) and the low-firing rate distribution (blue), respectively. However, a greater number of spikes is evoked by a strong whisking movement than by a weak one. Thus, the red and blue response probability distributions predict progressively higher firing rates as the strength of motor output goes from 0 to 1.

Let us assume an ideal 'decoder' of sensory signals that has perfect knowledge of the motor output. This would eliminate any uncertainty along the motor dimension, and the firing rate on any given trial would then be predicted by a 'slice' through the red and blue surfaces (FIG. 6a). The sharp separation between the rough and smooth response distributions enables efficient decoding. With the parameters chosen in the model, and provided that the decoder has exact knowledge of the motor output in every trial, $d' = 3.20$ and the information that is carried by the firing rate in each trial is 0.80 bits. One 'bit' corresponds to complete knowledge of the motor output in a task with two possible outcomes; a value of 0.8 bits means that the firing rate allows a correct inference of texture in 97% of trials. With complete motor knowledge, the intrinsic response variance is the only remaining source of uncertainty. This variance is reflected by the fact that even when an immobile animal passively receives repeated stimuli of an identical texture, neuronal responses differ across trials[49] due to the noise that is generated along the afferent pathway and to fluctuations in the excitability of the receiving cortical population[57,40].

If no knowledge of the motor output is available (FIG. 6b), the sensory response in any given trial must be decoded using the rough and smooth response distributions encompassing the full motor range; these are shown projected on the right wall of the graph. When neuronal responses from an awake, behaving rat are analysed with no independent signal from the motor system, the experimenter's decoding algorithms operate in this manner; this is the situation in the experiment depicted in FIG. 5. With the selected parameters of the model, $d' = 1$ and the information is 0.16 bits.

Texture decoding with an intermediate degree of motor knowledge (FIG. 6c) would occur in situations in which the barrel cortex receives information about whisking strength, but in which the received motor signal does not exactly match the actual whisker motion and/or cannot be perfectly integrated into the sensory system. In this case, the expected sensory response corresponds to a Gaussian-shaped slice through the two parallel elevations (FIG. 6c). The resulting response distributions are again projected on the right wall. In our model, $d' = 1.76$ and the information is 0.41 bits.

d′
(d prime). A measure of the discriminability of two stimuli. If the stimuli differ with respect to some quantity, d' is defined as the difference between the means divided by the standard deviations.

© 2008 Macmillan Publishers Limited. All rights reserved.

As the decoder has access to progressively greater knowledge about the whisking signal that evoked the sensory response, both d' and information (bits) about the texture increase (FIG. 6d). The model makes a precise prediction: as soon as we are be able to measure a rat's motor output, either by tracking the whiskers or by electromyography, we will be able to explain much of the trial-to-trial variation in the contact-evoked firing rate. Once we compensate for the variation created by the motor output, only the variation that is associated with the stimulus remains. This signal would be expected to give a much better read-out of the contacted object than the 'motor-ignorant' signal that has been analysed previously[6]. Although here the model was applied to texture discrimination, the main idea can be applied to any two distributions. For example, a high firing rate could encode contact with a pole or wall that is positioned close to the snout and a low firing rate could encode contact with an object that is located farther away from the snout (small and large radial distance, respectively).

How does the sensory system obtain knowledge of the executed movement? There are two possibilities. First, sensory pathways might receive copies of the motor signal from the brainstem, zona incerta, the cerebellum and the motor cortices[7,11,39,58,59]. Second, the sensory pathway itself might carry afferent signals about whisker motion through the whisking cells described above[29,36]. In general, anatomical and physiological evidence[60,61] indicates that the barrel cortex is a direct participant in the motor network (BOX 1).

Future directions

Along with continuing work on the fundamental mechanisms of synaptic integration (reviewed in REFS 12,13), three problems strike us as particularly important in understanding how the brain of actively whisking animals builds up a representation of the surrounding world.

The first problem is the characterization of how whisker dynamics are reported by neuronal activity in behaving animals. This problem is complex owing to the large number of mechanical parameters that define the state of the whisker (such as position, velocity, speed, acceleration and torque, all in three dimensions) and that could, potentially, be encoded by neurons. Different neurons might encode different features. Although there has been progress in quantifying which elements of natural whisker motion evoke spikes in the sensory pathways of anaesthetized animals[29,49,62], it has proven difficult to record a large enough number of spikes in awake rats and at the same time accurately monitor the whiskers. Neuroscientists have not yet identified in a rigorous, quantitative manner which features of the environment are reported by neurons of any sensory modality in an awake, freely moving mammal, but this is a realistic goal for researchers of the whisker sensory system.

As a second problem, we pose the question of whether the animal forms explicit representations of the identity of the things it touches ('what') and of the spatial coordinates of these things ('where') through separate cortical processing streams. In visual cortical processing, both the dorsal 'where' processing stream and the ventral 'what' processing stream use elemental information from the primary visual cortex about the orientation, size and shape of objects, and about their spatial relations. However, the two streams deal with the available visual information in different ways: the ventral stream transforms visual information into perceptual representations that embody the identifying features of objects — many inferotemporal neurons respond to the identity of a face even if the visual field position or viewing angle of the face is altered[63]. In parallel, the dorsal stream transforms visual information into representations of the configuration of objects within egocentric frames of reference, thereby mediating goal-directed acts[64]. Likewise, in whisker-mediated touch, the same information supports knowledge of object identity and spatial coordinates. Suppose a rat learns that food is located behind a sphere but not behind a cube. Discrimination between the two objects derives from the horizontal, radial and vertical location of contact during the whisk. Thus, spatial coordinates translate to an object's identity as a sphere or cube. Yet the same coordinates translate to object location and thereby instruct the animal's quickest pathway around the object to the food. By analogy with vision, within 'what' and 'where' processing streams in touch, the neuronal response to features of one type will not be affected by changes in features of the other type. Our prediction is that in stations along the 'what' pathway, neurons will be found to encode 'cube' or 'sphere' independently of the objects' spatial coordinates, whereas in stations along the 'where' pathway, neurons might encode 'move left' or 'move right' independently of the object's identity. Both streams would contribute to the general transformation of neuronal representations from stages at which they encode physical signals to stages at which they encode the identity of an object and the actions required by the presence of that object. Where in the whisker system such separation begins is an open question[19]. Emergence of functional streams from higher-order cortical processing is one possibility, but an alternative possibility needs to be considered: the richly varying assortment of receptors in the follicle make it a possible starting place for separate functional streams. Some receptor types may generate signals that are crucial for one functional stream but not the other.

The third problem, which is inseparable from the first two, is to elucidate how neuronal representations are transformed from stages at which they encode physical signals to stages at which they encode things that are meaningful to the animal. What matters to the survival of a rodent, after all, is not only the capacity of its neurons to encode whisker kinetics, but also the ability to determine the identity of the object that induced the kinetics — mouse trap or cheese? It has been argued convincingly that this transformation is a primary function of cortical processing[65]. The work reviewed here has begun to shed light on how cortical neurons represent the location and characteristic features of a contacted object. It will be exciting to build on this, proceeding from the study of how the brain encodes elemental properties to how it encodes the higher-level, more abstract meaning of a stimulus — its category, its value and the action that must be taken.

Electromyography
Recording of electrical activity generated by the muscle

© 2008 Macmillan Publishers Limited. All rights reserved.

1. Vincent, S. B. The function of vibrissae in the behavior of the white rat. *Behavior. Mon.* **1**, 1–82 (1912).
Classic study, approaching its 100th anniversary, demonstrating for the first time the behavioural importance of whiskers: in maze navigation, rats became slow and prone to errors after whisker clipping.
2. Brecht, M., Preilowski, B. & Merzenich, M. M. Functional architecture of the mystacial vibrissae. *Behav. Brain Res.* **84**, 81–97 (1997).
This paper provided the first morphological and functional distinction between micro- and macrovibrissae.
3. Carvell, G. E. & Simons, D. J. Biometric analyses of vibrissal tactile discrimination in the rat. *J. Neurosci.* **10**, 2638–2648 (1990).
First quantification of whisking frequency and speed during the discrimination of textures.
4. Guic-Robles, E., Valdivieso, C. & Guajardo, G. Rats can learn a roughness discrimination using only their vibrissal system. *Behav. Brain Res.* **31**, 285–289 (1989).
5. Prigg, T., Goldreich, D., Carvell, G. E. & Simons, D. J. Texture discrimination and unit recordings in the rat whisker/barrel system. *Physiol. Behav.* **77**, 671–675 (2002).
6. von Heimendahl, M., Itskov, P. M., Arabzadeh, E. & Diamond, M. E. Neuronal activity in rat barrel cortex underlying texture discrimination. *PLoS Biol.* **5**, e305 (2007).
This was the first study to characterize the response differences in the barrel cortex that are associated with two stimuli during tactile discrimination. The analysis showed how trial-to-trial variations in neuronal activity correlated with the animal's percept.
7. Berg, R. W. & Kleinfeld, D. Rhythmic whisking by rat: retraction as well as protraction of the vibrissae is under active muscular control. *J. Neurophysiol.* **89**, 104–117 (2003).
8. Hill, D. N., Bermejo, R., Zeigler, H. P. & Kleinfeld, D. Biomechanics of the vibrissa motor plant in rat: rhythmic whisking consists of triphasic neuromuscular activity. *J. Neurosci.* **28**, 3438–3455 (2008).
Provides a detailed model for how muscle contraction is translated into whisker movement.
9. Mitchinson, B., Martin, C. J., Grant, R. A. & Prescott, T. J. Feedback control in active sensing: rat exploratory whisking is modulated by environmental contact. *Proc. Biol. Sci.* **274**, 1035–1041 (2007).
10. Hartmann, M. Active sensing capabilities of the rat whisker system. *Autonomous Robots* **11**, 249–254 (2001).
11. Kleinfeld, D., Ahissar, E. & Diamond, M. E. Active sensation: insights from the rodent vibrissa sensorimotor system. *Curr. Opin. Neurobiol.* **16**, 435–444 (2006).
This review summarizes current knowledge regarding the anatomical and physiological interplay between sensory and motor systems.
12. Petersen, C. C. H. The functional organization of the barrel cortex. *Neuron* **56**, 339–355 (2007).
13. Brecht, M. Barrel cortex and whisker-mediated behaviors. *Curr. Opin. Neurobiol.* **17**, 408–416 (2007).
14. Dörfl, J. The innervation of the mystacial region of the white mouse: A topographical study. *J. Anat.* **142**, 173–184 (1985).
15. Torvik, A. Afferent connections to the sensory trigeminal nuclei, the nucleus of the solitary tract and adjacent structures; an experimental study in the rat. *J. Comp. Neurol.* **106**, 51–141 (1956).
16. Clarke, W. B. & Bowsher, D. Terminal distribution of primary afferent trigeminal fibers in the rat. *Exp. Neurol.* **6**, 372–383 (1962).
17. Deschênes, M., Timofeeva, E., Lavallée, P. & Dufresne, C. The vibrissal system as a model of thalamic operations. *Prog. Brain Res.* **149**, 31–40 (2005).
18. Woolsey, T. A. & van der Loos, H. The structural organization of layer iv in the somatosensory region (si) of mouse cerebral cortex. the description of a cortical field composed of discrete cytoarchitectonic units. *Brain Res.* **17**, 205–242 (1970).
19. Alloway, K. D. Information processing streams in rodent barrel cortex: the differential functions of barrel and septal circuits. *Cereb. Cortex* **18**, 979–989 (2008).
20. Hutson, K. A. & Masterton, R. B. The sensory contribution of a single vibrissa's cortical barrel. *J. Neurophysiol.* **56**, 1196–1223 (1986).
This classic paper presents a spatial task that can be performed without visual input and proves that rats require an intact pathway from one whisker to one cortical barrel in order to perform the task.
21. Jenkinson, E. W. & Glickstein, M. Whiskers, barrels, and cortical efferent pathways in gap crossing by rats. *J. Neurophysiol.* **84**, 1781–1789 (2000).
22. Schiffman, H. R., Lore, R., Passafiume, J. & Neeb, R. Role of vibrissae for depth perception in the rat (rattus norvegicus). *Anim. Behav.* **18**, 290–292 (1970).
23. Krupa, D. J., Matell, M. S., Brisben, A. J., Oliveira, L. M. & Nicolelis, M. A. Behavioral properties of the trigeminal somatosensory system in rats performing whisker-dependent tactile discriminations. *J. Neurosci.* **21**, 5752–5763 (2001).
24. Shuler, M. G., Krupa, D. J. & Nicolelis, M. A. L. Integration of bilateral whisker stimuli in rats: role of the whisker barrel cortices. *Cereb. Cortex* **12**, 86–97 (2002).
25. Knutsen, P. M., Pietr, M. & Ahissar, E. Haptic object localization in the vibrissal system: behavior and performance. *J. Neurosci.* **26**, 8451–8464 (2006).
26. Harris, J. A., Petersen, R. S. & Diamond, M. E. Distribution of tactile learning and its neural basis. *Proc. Natl Acad. Sci. USA* **96**, 7587–7591 (1999).
27. Mehta, S. B., Whitmer, D., Figueroa, R., Williams, B. A. & Kleinfeld, D. Active spatial perception in the vibrissa scanning sensorimotor system. *PLoS Biol.* **5**, e15 (2007).
This study measures the capacity of rats to localize an object in the horizontal dimension using a single whisker in an absolute coordinate system. The paper has important implications for understanding the rat's knowledge of its own whisker position.
28. Fee, M. S., Mitra, P. P. & Kleinfeld, D. Central versus peripheral determinants of patterned spike activity in rat vibrissa cortex during whisking. *J. Neurophysiol.* **78**, 1144–1149 (1997).
29. Szwed, M., Bagdasarian, K. & Ahissar, E. Encoding of vibrissal active touch. *Neuron* **40**, 621–630 (2003).
30. Ahissar, E. & Arieli, A. Figuring space by time. *Neuron* **32**, 185–201 (2001).
31. Westheimer, G. & McKee, S. Spatial configurations for visual hyperacuity. *Vision Res.* **17**, 941–947 (1977).
32. Szwed, M. *et al.* Responses of trigeminal ganglion neurons to the radial distance of contact during active vibrissal touch. *J. Neurophysiol.* **95**, 791–802 (2006).
33. Leiser, S. C. & Moxon, K. A. Responses of trigeminal ganglion neurons during natural whisking behaviors in the awake rat. *Neuron* **53**, 117–133 (2007).
34. Solomon, J. H. & Hartmann, M. J. Biomechanics: Robotic whiskers used to sense features. *Nature* **443**, 525–525 (2006).
35. Mehta, S. B. & Kleinfeld, D. Frisking the whiskers: patterned sensory input in the rat vibrissa system. *Neuron* **41**, 181–184 (2004).
36. Yu, C., Derdikman, D., Haidarliu, S. & Ahissar, E. Parallel thalamic pathways for whisking and touch signals in the rat. *PLoS Biol.* **4**, e124 (2006).
This study shows that the whisking and contact response segregation, first found in trigeminal ganglion cells, extends through distinct thalamic nuclei.
37. Derdikman, D. *et al.* Layer-specific touch-dependent facilitation and depression in the somatosensory cortex during active whisking. *J. Neurosci.* **26**, 9538–9547 (2006).
38. Brecht, M. & Sakmann, B. Dynamic representation of whisker deflection by synaptic potentials in spiny stellate and pyramidal cells in the barrels and septa of layer 4 rat somatosensory cortex. *J. Physiol.* **543**, 49–70 (2002).
39. Hentschke, H., Haiss, F. & Schwarz, C. Central signals rapidly switch tactile processing in rat barrel cortex during whisker movements. *Cereb. Cortex* **16**, 1142–1156 (2006).
40. Crochet, S. & Petersen, C. C. H. Correlating whisker behavior with membrane potential in barrel cortex of awake mice. *Nature Neurosci.* **9**, 608–610 (2006).
41. O'Connor, S. M., Berg, R. W. & Kleinfeld, D. Coherent electrical activity between vibrissa sensory areas of cerebellum and neocortex is enhanced during free whisking. *J. Neurophysiol.* **87**, 2137–2148 (2002).
42. Ganguly, K. & Kleinfeld, D. Goal-directed whisking increases phase-locking between vibrissa movement and electrical activity in primary sensory cortex in rat. *Proc. Natl Acad. Sci. USA* **101**, 12348–12353 (2004).
43. Ferezou, I., Bolea, S. & Petersen, C. C. H. Visualizing the cortical representation of whisker touch: voltage-sensitive dye imaging in freely moving mice. *Neuron* **50**, 617–629 (2006).
The spatial and temporal distribution of activity evoked by whisker movement in an awake mouse is not constant over time but varies dramatically according to the ongoing behaviour of the animal.
44. Curtis, J. C. & Kleinfeld, D. Seeing what the mouse sees with its vibrissae: a matter of behavioral state. *Neuron* **50**, 524–526 (2006).
45. Anjum, F., Turni, H., Mulder, P. G. H., van der Burg, J. & Brecht, M. Tactile guidance of prey capture in etruscan shrews. *Proc. Natl Acad. Sci. USA* **103**, 16544–16549 (2006).
46. Barnett, S. A. Ecology. In Wishaw, I. Q. & Kolb, B. (eds.) *The behavior of the laboratory rat*, 15–24 (Oxford University Press, 2005).
47. Lamb, G. D. Tactile discrimination of textured surfaces: psychophysical performance measurements in humans. *J. Physiol.* **338**, 551–565 (1983).
48. Morley, J. W., Goodwin, A. W. & Darian-Smith, I. Tactile discrimination of gratings. *Exp. Brain Res.* **49**, 291–299 (1983).
49. Arabzadeh, E., Zorzin, E. & Diamond, M. E. Neuronal encoding of texture in the whisker sensory pathway. *PLoS Biol.* **3**, e17 (2005).
This study used the electrical whisking paradigm to show distinctive motion profiles as the whisker swept along various textures. Neurons in the trigeminal ganglion and in barrel cortex encoded textures by firing for high-velocity events.
50. Hipp, J. *et al.* Texture signals in whisker vibrations. *J. Neurophysiol.* **95**, 1792–1799 (2006).
51. Arabzadeh, E., Panzeri, S. & Diamond, M. E. Deciphering the spike train of a sensory neuron: counts and temporal patterns in the rat whisker pathway. *J. Neurosci.* **26**, 9216–9226 (2006).
Using data collected previsouly (reference 49), this paper quantified two different ways in which neuronal activity could carry information to distinguish textures — the number of spikes accumulated in each whisk (firing rate) and the relative timing of spikes across the whisk (firing pattern).
52. Luna, R., Hernández, A., Brody, C. D. & Romo, R. Neural codes for perceptual discrimination in primary somatosensory cortex. *Nature Neurosci.* **8**, 1210–1219 (2005).
This study evaluated potential vibration-coding mechanisms in the monkey cortex by comparing the performance of each candidate code across a single trial with the animal's performance on the same trial.
53. Ritt, J. T., Andermann, M. L. & Moore, C. I. Embodied information processing: vibrissa mechanics and texture features shape micromotions in actively sensing rats. *Neuron* **57**, 599–613 (2008).
54. Diamond, M. E., Arabzadeh, E. & von Heimendahl, M. Whisker-mediated texture discrimination. *PloS Biol.* (in the press).
55. Diamond, M. E., von Heimendahl, M. & Arabzadeh, E. Whisker kinetics: What does the rat's brain listen to? *Neuron* (in the press).
56. Gamzu, E. & Ahissar, E. Importance of temporal cues for tactile spatial- frequency discrimination. *J. Neurosci.* **21**, 7416–7427 (2001).
57. Erchova, I. A. & Diamond, M. E. Rapid fluctuations in rat barrel cortex plasticity. *J. Neurosci.* **24**, 5931–5941 (2004).
58. Ahrens, K. F. & Kleinfeld, D. Current flow in vibrissa motor cortex can phase-lock with exploratory rhythmic whisking in rat. *J. Neurophysiol.* **92**, 1700–1707 (2004).
59. Veinante, P. & Deschênes, M. Single-cell study of motor cortex projections to the barrel field in rats. *J. Comp. Neurol.* **464**, 98–103 (2003).
60. Gioanni, Y. & Lamarche, M. A reappraisal of rat motor cortex organization by intracortical microstimulation. *Brain Res.* **344**, 49–61 (1985).
61. Kleinfeld, D., Sachdev, R. N. S., Merchant, L. M., Jarvis, M. R. & Ebner, F. F. Adaptive filtering of vibrissa input in motor cortex of rat. *Neuron* **34**, 1021–1034 (2002).
62. Ferezou, I. *et al.* Spatiotemporal dynamics of cortical sensorimotor integration in behaving mice. *Neuron* **56**, 907–923 (2007).
63. Afraz, S.-R., Kiani, R. & Esteky, H. Microstimulation of inferotemporal cortex influences face categorization. *Nature* **442**, 692–695 (2006).
64. Goodale, M. A., Milner, A. D., Jakobson, L. S. & Carey, D. P. A neurological dissociation between

© 2008 Macmillan Publishers Limited. All rights reserved.

perceiving objects and grasping them. *Nature* **349**, 154–156 (1991).
65. Whitfield, I. C. The object of the sensory cortex. *Brain Behav. Evol.* **16**, 129–154 (1979).
This monograph presents an elegant and general theory for the transformation of sensory-perceptual representations by intracortical processing streams.
66. Lorente de Nó, R. La corteza cerebral del raton. *Trab. Laboratory Invest. Bio. (Madrid)* **20**, 41–78 (1922).
67. Killackey, H. P. Anatomical evidence for cortical subdivisions based on vertically discrete thalamic projections from the ventral posterior nucleus to cortical barrels in the rat. *Brain Res.* **51**, 326–331 (1973).
68. Pierret, T., Lavallée, P. & Deschênes, M. Parallel streams for the relay of vibrissal information through thalamic barreloids. *J. Neurosci.* **20**, 7455–7462 (2000).
69. Furuta, T., Nakamura, K. & Deschenes, M. Angular tuning bias of vibrissa-responsive cells in the paralemniscal pathway. *J. Neurosci.* **26**, 10548–10557 (2006).
70. Veinante, P., Jacquin, M. F. & Deschênes, M. Thalamic projections from the whisker-sensitive regions of the spinal trigeminal complex in the rat. *J. Comp. Neurol.* **420**, 233–243 (2000).
71. Koralek, K. A., Jensen, K. F. & Killackey, H. P. Evidence for two complementary patterns of thalamic input to the rat somatosensory cortex. *Brain Res.* **463**, 346–351 (1988).
72. Lu, S. M. & Lin, R. C. Thalamic afferents of the rat barrel cortex: a light- and electron-microscopic study using phaseolus vulgaris leucoagglutinin as an anterograde tracer. *Somatosens. Mot. Res.* **10**, 1–16 (1993).
73. Bureau, I., von Saint Paul, F. & Svoboda, K. Interdigitated paralemniscal and lemniscal pathways in the mouse barrel cortex. *PLoS Biol.* **4**, e382 (2006).
74 Carvell, G. E. & Simons, D. J. Thalamic and corticocortical connections of the second somatic sensory area of the mouse. *J. Comp. Neurol.* **265**, 409–427 (1987).
75 Alloway, K. D., Mutic, J. J., Hoffer, Z. S. & Hoover, J. E. Overlapping corticostriatal projections from the rodent vibrissal representations in primary and secondary somatosensory cortex. *J. Comp. Neurol.* **428**, 51–67 (2000).
76. Castro-Alamancos, M. A. & Connors, B. W. Thalamocortical synapses. *Prog. Neurobiol.* **51**, 581–606 (1997).
77. Diamond, M. E., Armstrong-James, M. & Ebner, F. F. Somatic sensory responses in the rostral sector of the posterior group (pom) and in the ventral posterior medial nucleus (vpm) of the rat thalamus. *J. Comp. Neurol.* **318**, 462–476 (1992).
78. Ahissar, E., Sosnik, R. & Haidarliu, S. Transformation from temporal to rate coding in a somatosensory thalamocortical pathway. *Nature* **406**, 302–306 (2000).
79. Urbain, N. & Deschênes, M. A new thalamic pathway of vibrissal information modulated by the motor cortex. *J. Neurosci.* **27**, 12407–12412 (2007).
This paper presents the discovery of a pathway through the zona incerta that is involved specifically in the merging of sensory and motor signals.
80. Ahissar, E., Sosnik, R., Bagdasarian, K. & Haidarliu, S. Temporal frequency of whisker movement. ii. laminar organization of cortical representations. *J. Neurophysiol.* **86**, 354–367 (2001).
81. Golomb, D., Ahissar, E. & Kleinfeld, D. Coding of stimulus frequency by latency in thalamic networks through the interplay of gabab-mediated feedback and stimulus shape. *J. Neurophysiol.* **95**, 1735–1750 (2006).
82. Ghazanfar, A. A. & Nicolelis, M. A. Nonlinear processing of tactile information in the thalamocortical loop. *J. Neurophysiol.* **78**, 506–510 (1997).

Acknowledgements
The authors would like to thank their many brilliant and helpful colleagues, too numerous to list. The joint efforts of the senior authors (M.E.D., D.K. and E.A.) have been supported by Human Frontier Science Program grant RG0043/2004-C. M. E. D. additionally recognizes the support of EC grant BIOTACT (ICT-215910), Ministero per l'Istruzione, l'Università e la Ricerca grant 2006050482_003, Regione Friuli Venezia Giulia and the Italian Institute of Technology.

FURTHER INFORMATION
Mathew Diamond's homepage: www.sissa.it/cns/tactile

SUPPLEMENTARY INFORMATION
See online article: S1 (movie)

ALL LINKS ARE ACTIVE IN THE ONLINE PDF.

© 2008 Macmillan Publishers Limited. All rights reserved.

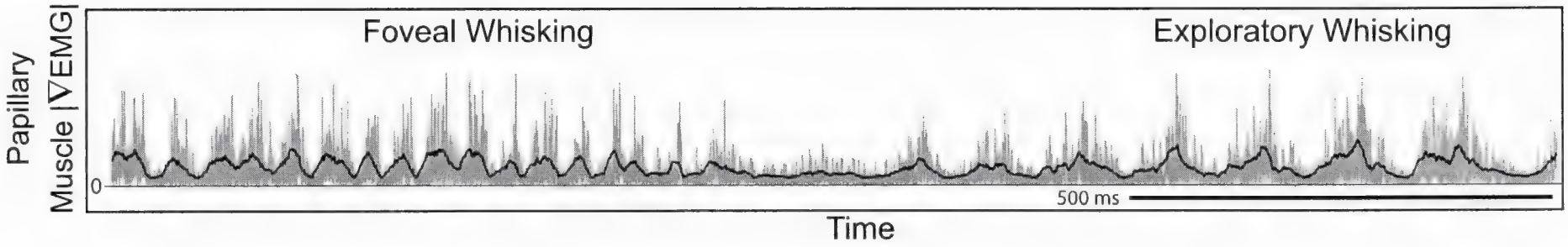
Motor control in the vibrissa scanning sensorimotor system

David Kleinfeld, UCSD

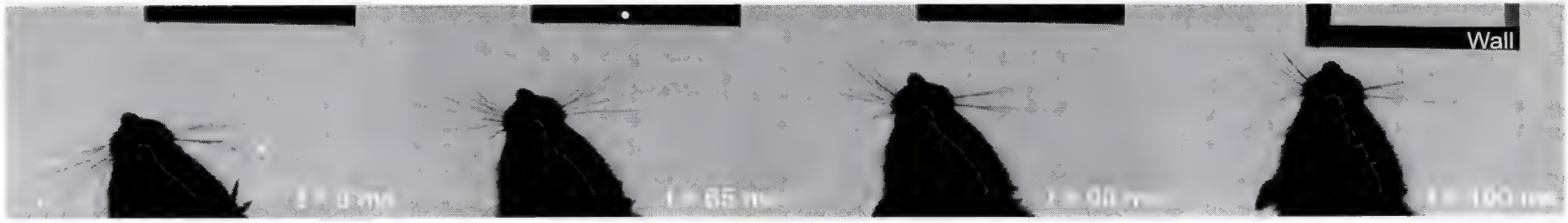
MBL August 2009
Methods in Computational Neuroscience

Modes of whisking by rat

Exploratory whisking, also referred to as symmetric whisking



Asymmetric whisking as a result of contact between the vibrissae and a wall



Berg and Kleinfeld (2003)
Towal and Hartmann (2006)
Mitchinson, Martin, Grant and Prescott (2007)

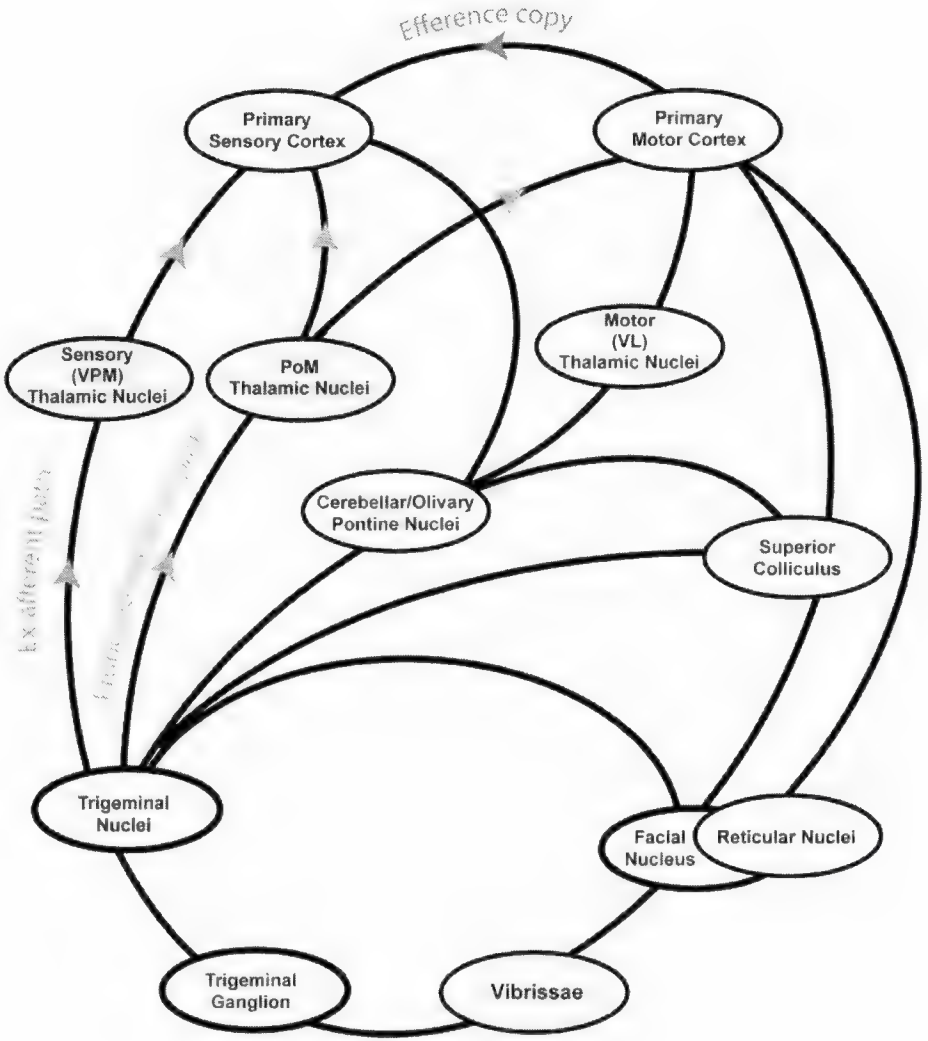
Understanding motor control is essential to decoding sensory input

"… [one cannot hope to understand sensation without consideration of the effects] produced on the sensory-receptors by the motor impulses which initiate a muscular movement" (von Holst, 1954)

Ex-afference - originates from environmental influences, *e.g.*, pressure for the case of touching.

Reafference - originates from motor activation of sensory receptors.
Peripheral reafference - same receptors encode motor activation and external stimuli.

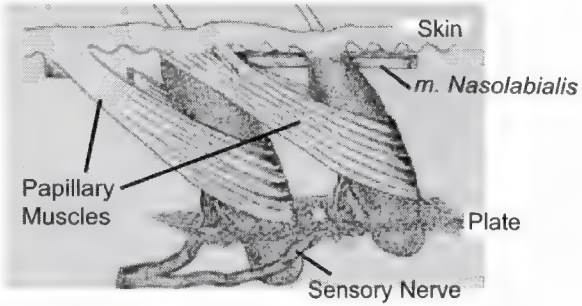
Ex-afference and reafference in the vibrissa scanning system

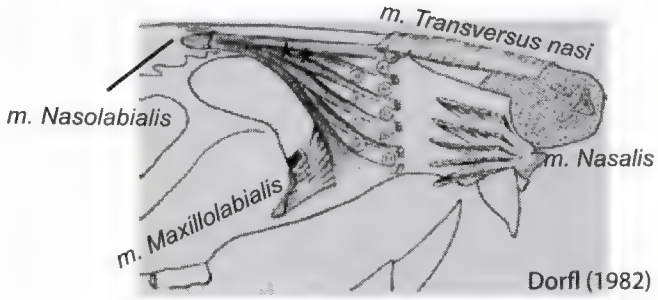


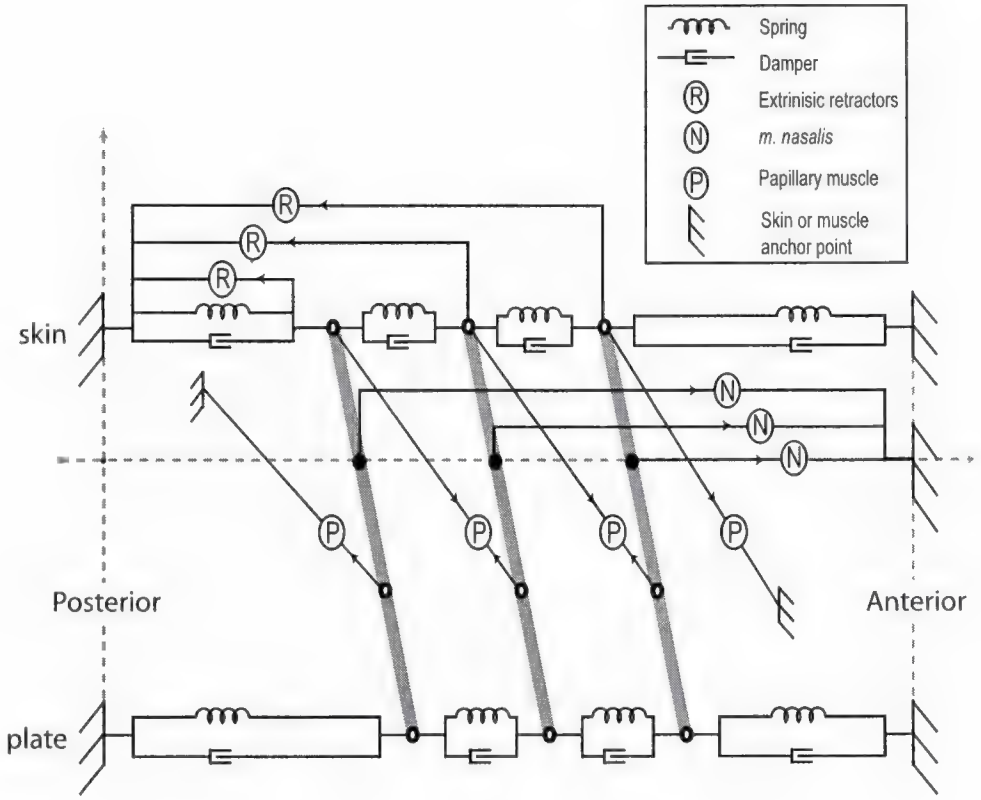
Motor control in the vibrissa scanning sensorimotor system

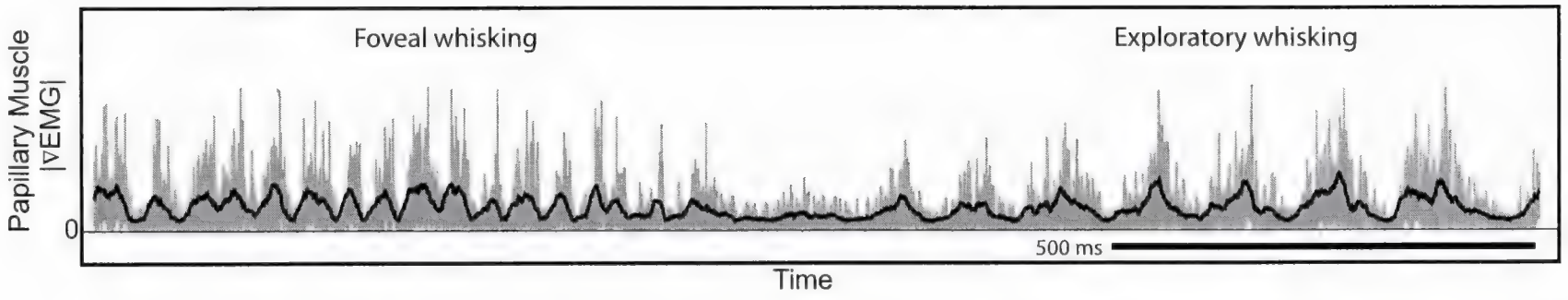
- **Phenomenology of whisking**
- Anatomy and physiology of facial motoneurons
- Multi-phasic and multi-level control of whisking
- Brainstem sensorimotor feedback

The motor plant consists of papillary (intrinsic) and extrinsic muscles that control exploratory (5 - 15 Hz) and foveal (15 - 25 Hz) whisking



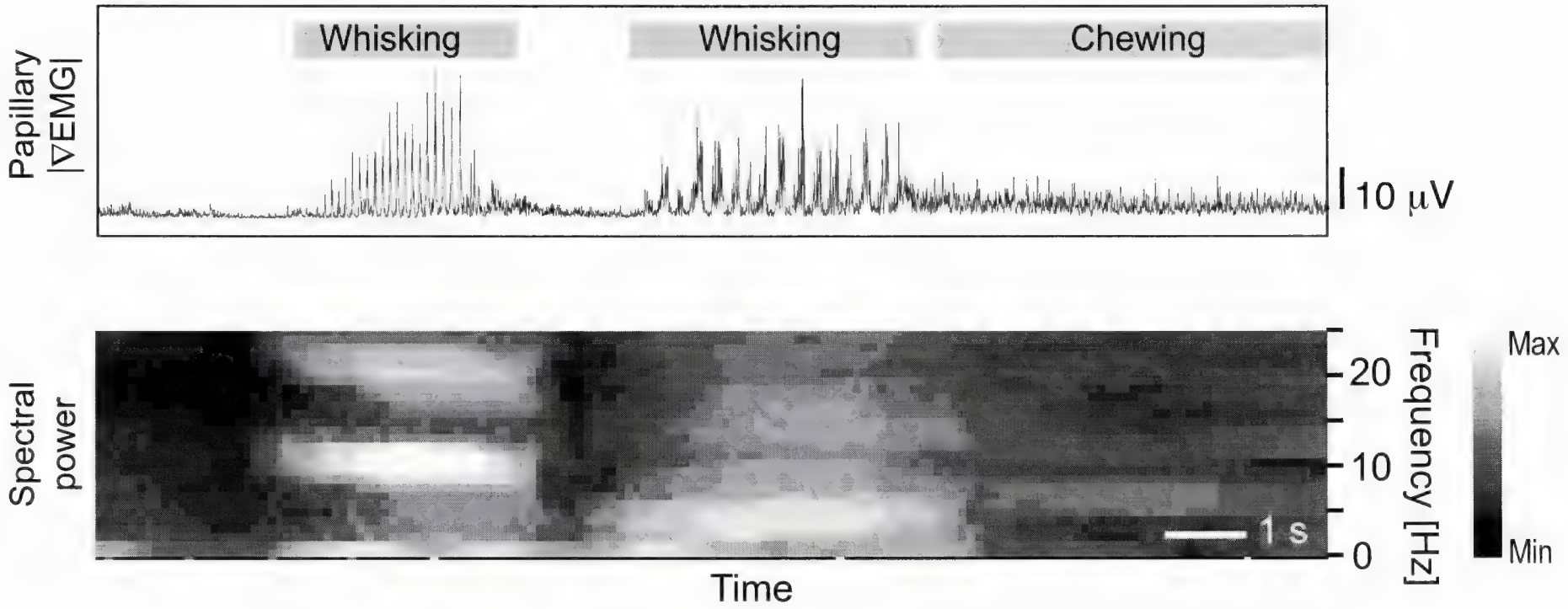






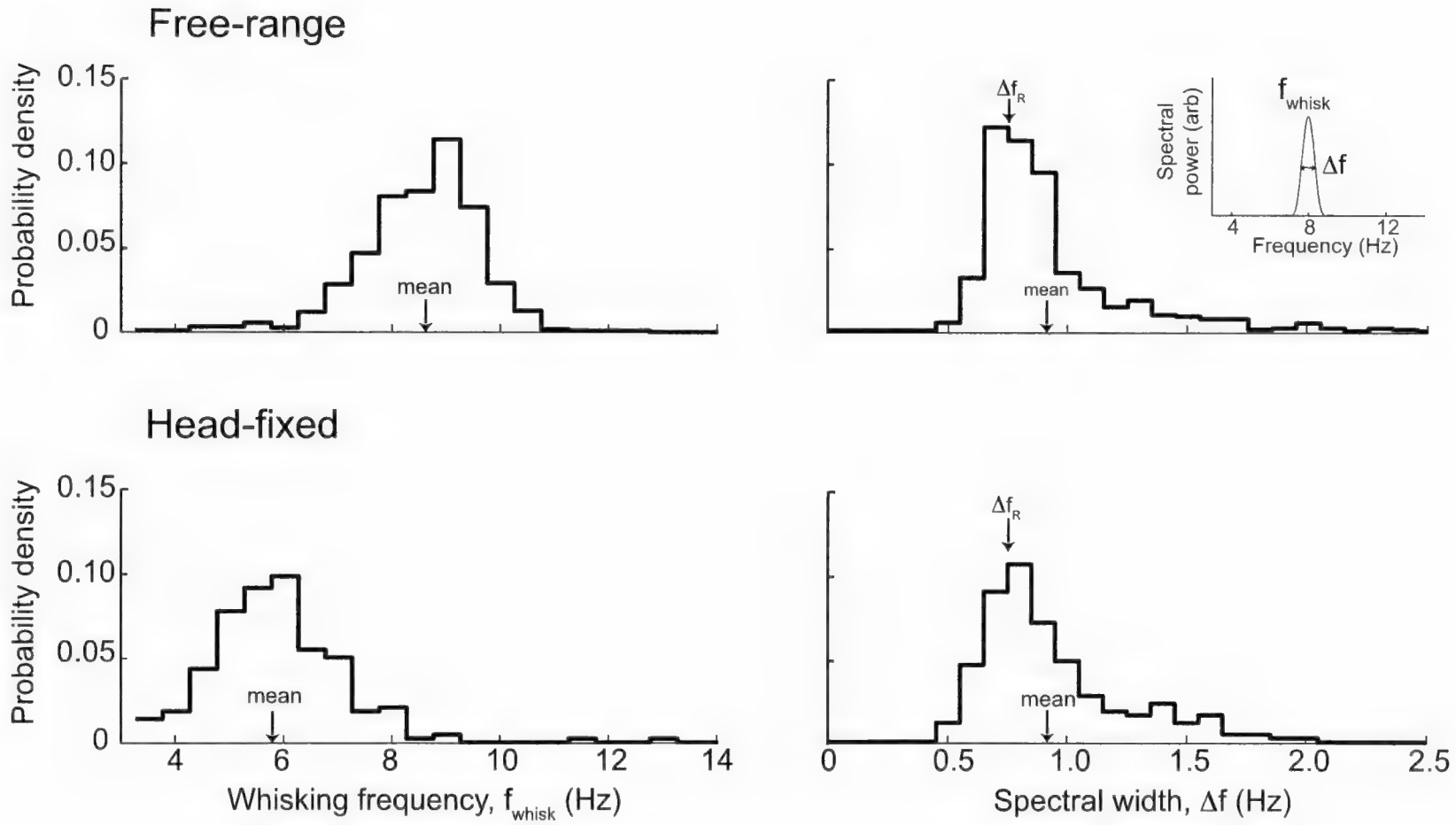
Berg and Kleinfeld (2003); Hill, Bermejo, Zeigler and Kleinfeld (2008)

Frequency of whisking is constant within a bout but changes from bout to bout



O'Connor, Berg and Kleinfeld (2001)

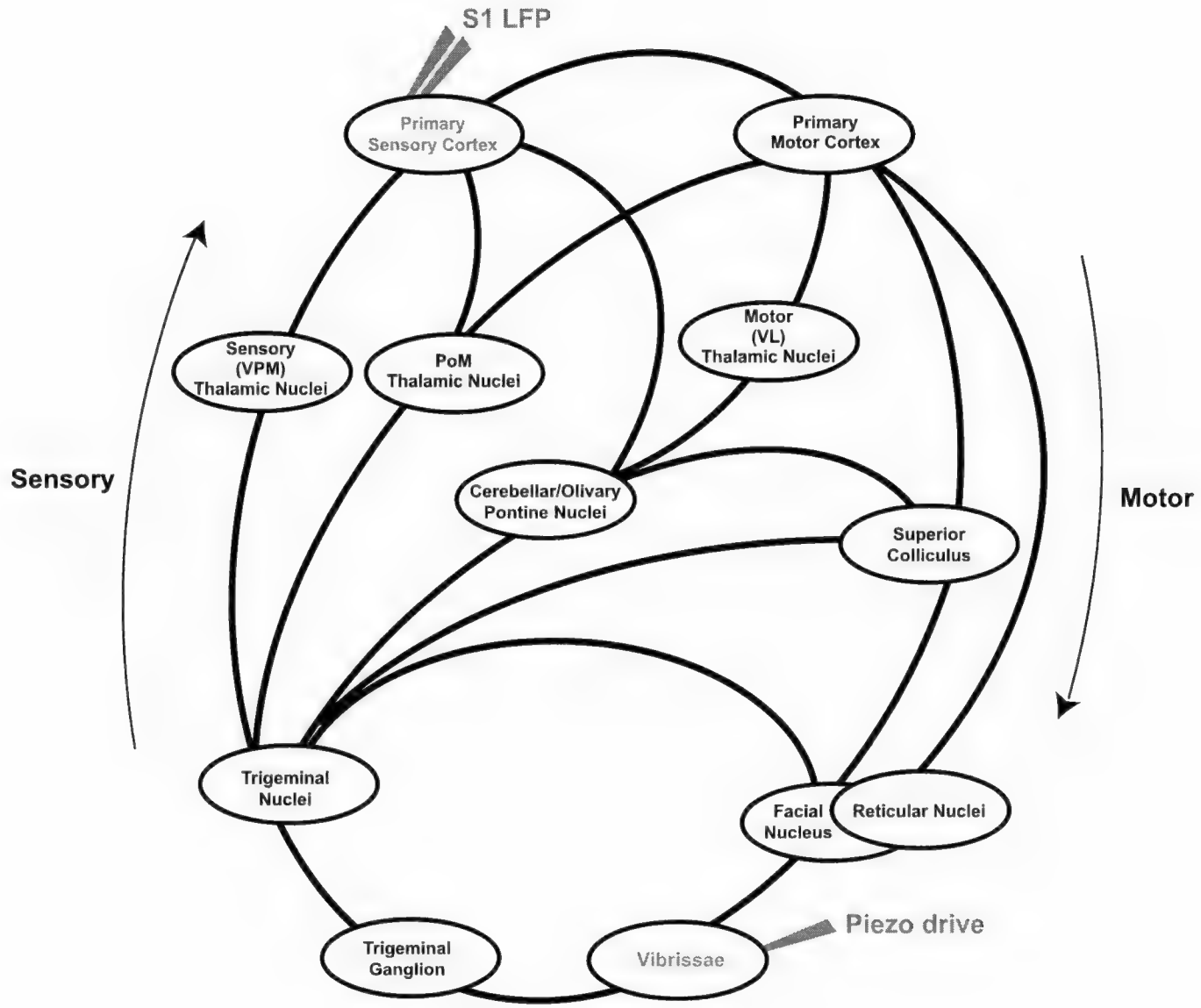
Exploratory whisking can occur at the theoretical limit of spectral purity



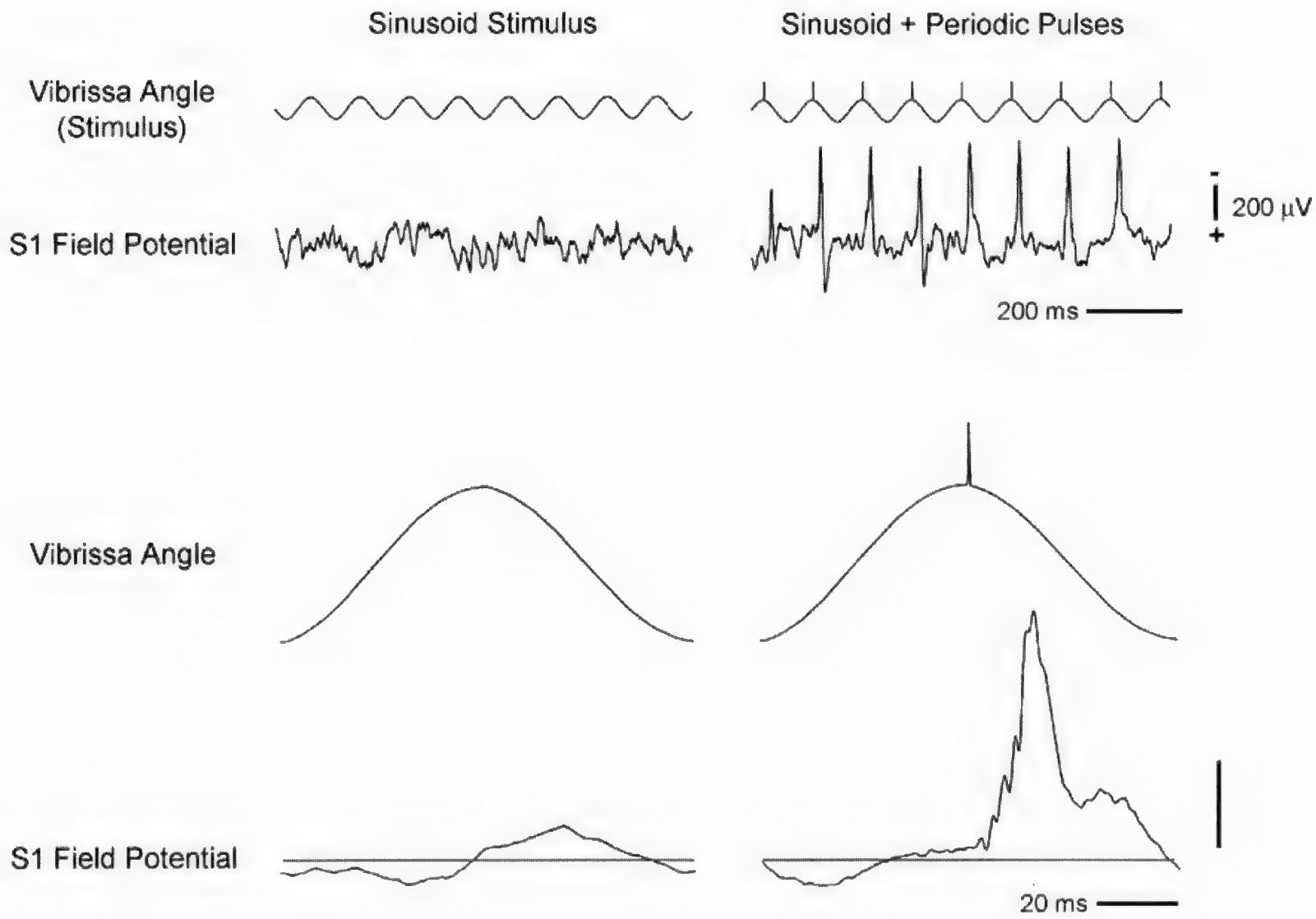
Implies that drive is described as $\cos\{2\pi \mathbf{f_{whisk}} t - \phi_{whisk}\} + \ldots$

Berg and Kleinfeld (2003); Hill, Bermejo, Zeigler and Kleinfeld (2008)

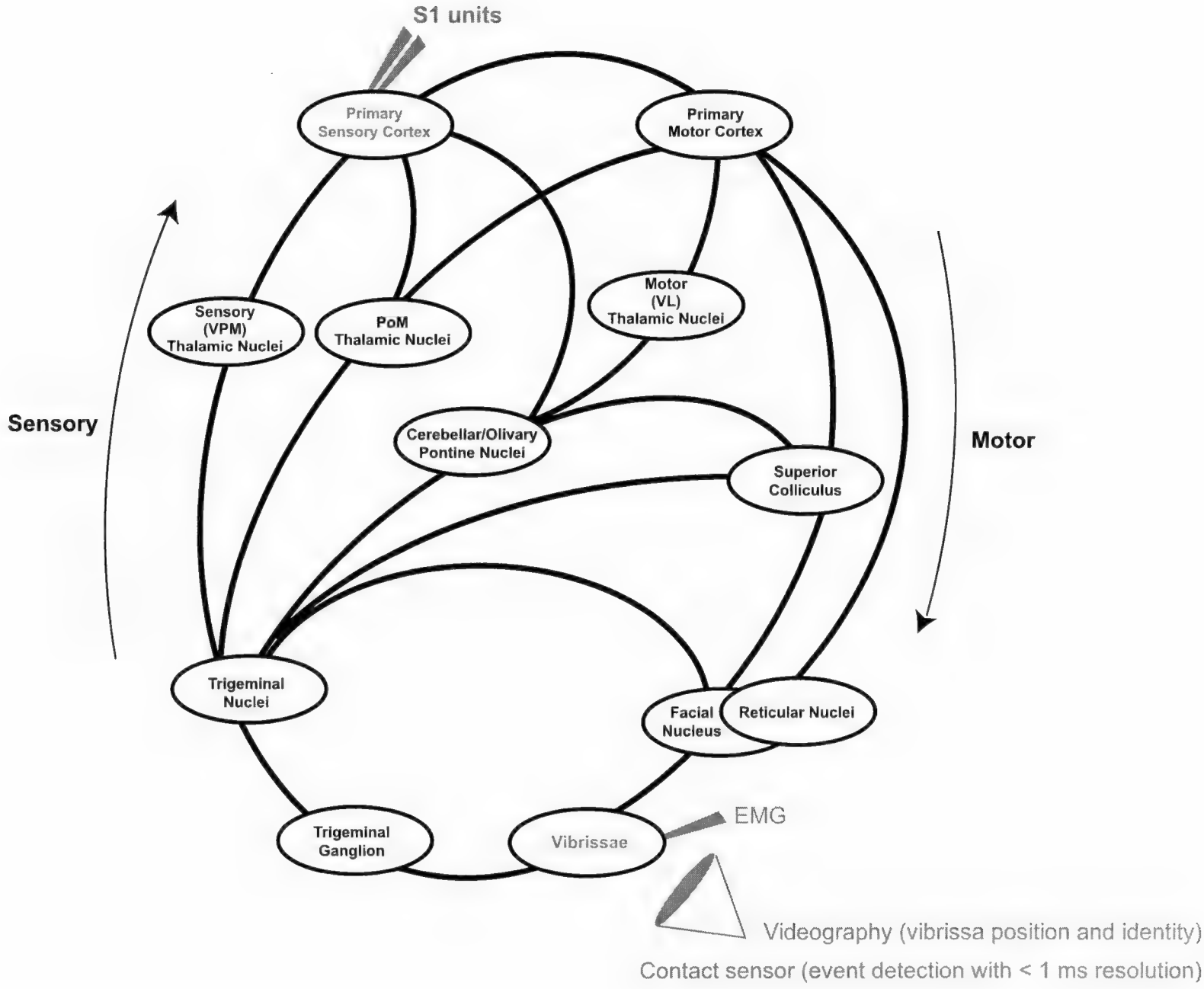
Relation of field potential in S1 cortex to passive motion of the vibrissae



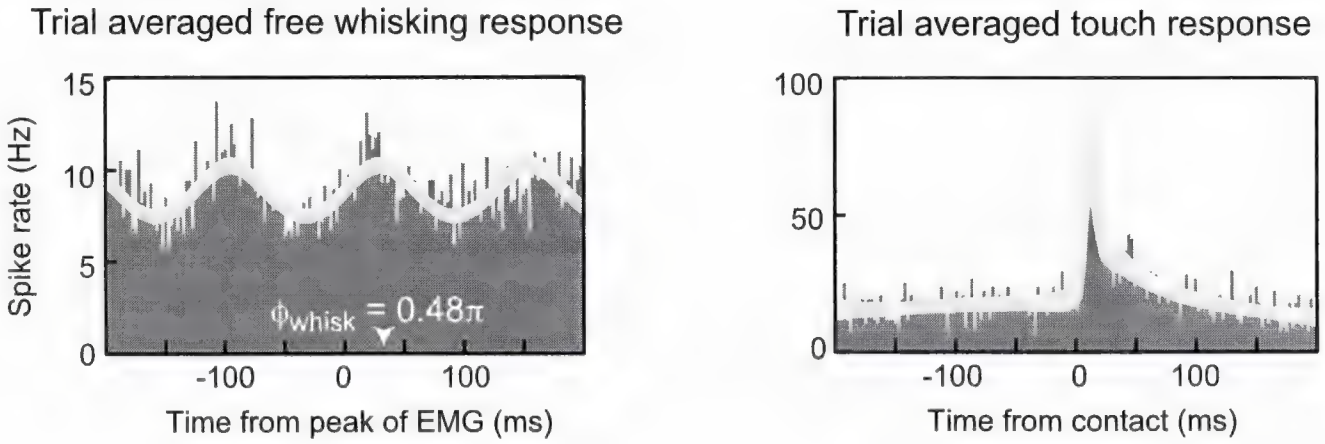
Coding of vibrissa motion is spectrally separate from coding of touch (Jones and Barth 1999)



Relation of spike response in S1 to position in the whisk cycle and touch

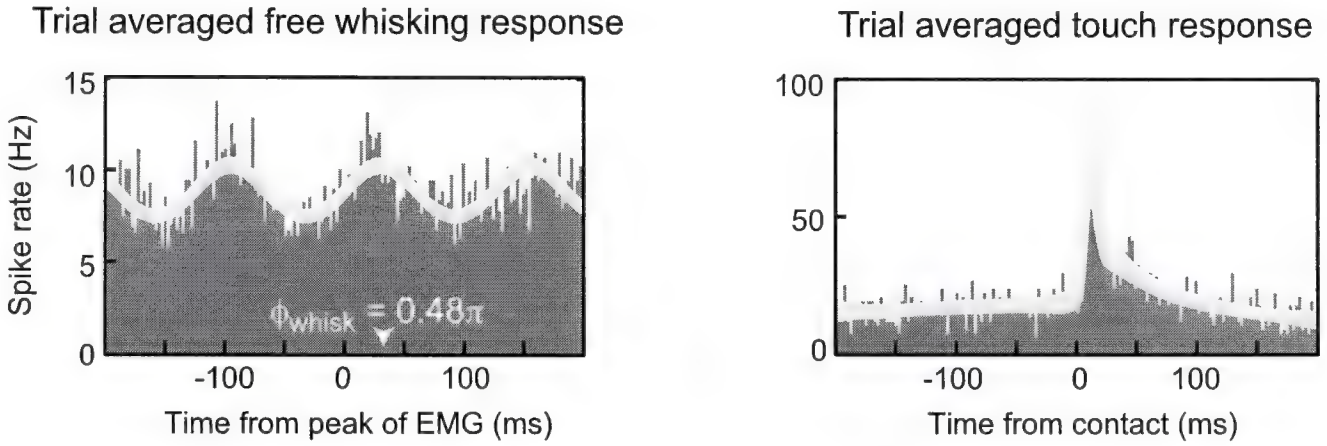


Coding of vibrissa motion is spectrally separate from coding of touch



Curtis and Kleinfeld (2009)

Coding of vibrissa motion is spectrally separate from coding of touch



We will return to this experimental result later in the context of coding object location

Curtis and Kleinfeld (2009)

Lesson 1

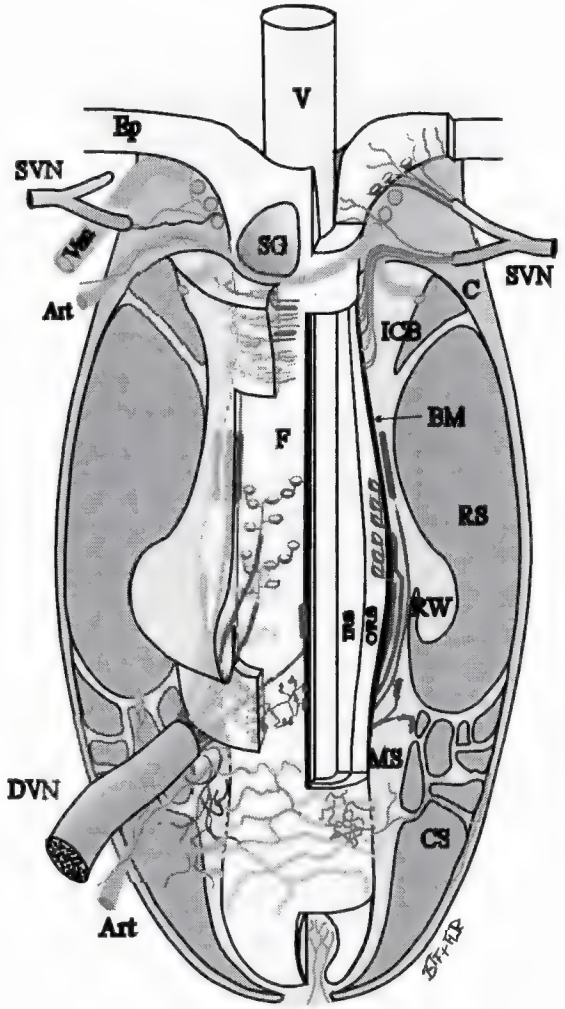
Whisking can be spectrally pure and mechanically smooth

Acts to decouple reafferent (whisking) from exafferent (touch) input

Query

How is self-motion versus touch coded in receptor subtypes?

Rice's conjecture (2001): Mechanical properties and innervation of the vibrissa follicle lead to separate position versus touch signals



Myelinated Mechanoreceptors:

- Transverse lanceolate endings
- Merkel cells and endings
- Lanceolate endings
- Reticular endings
- Fuzzy endings
- Club endings

Unmyelinated CGRP Endings:

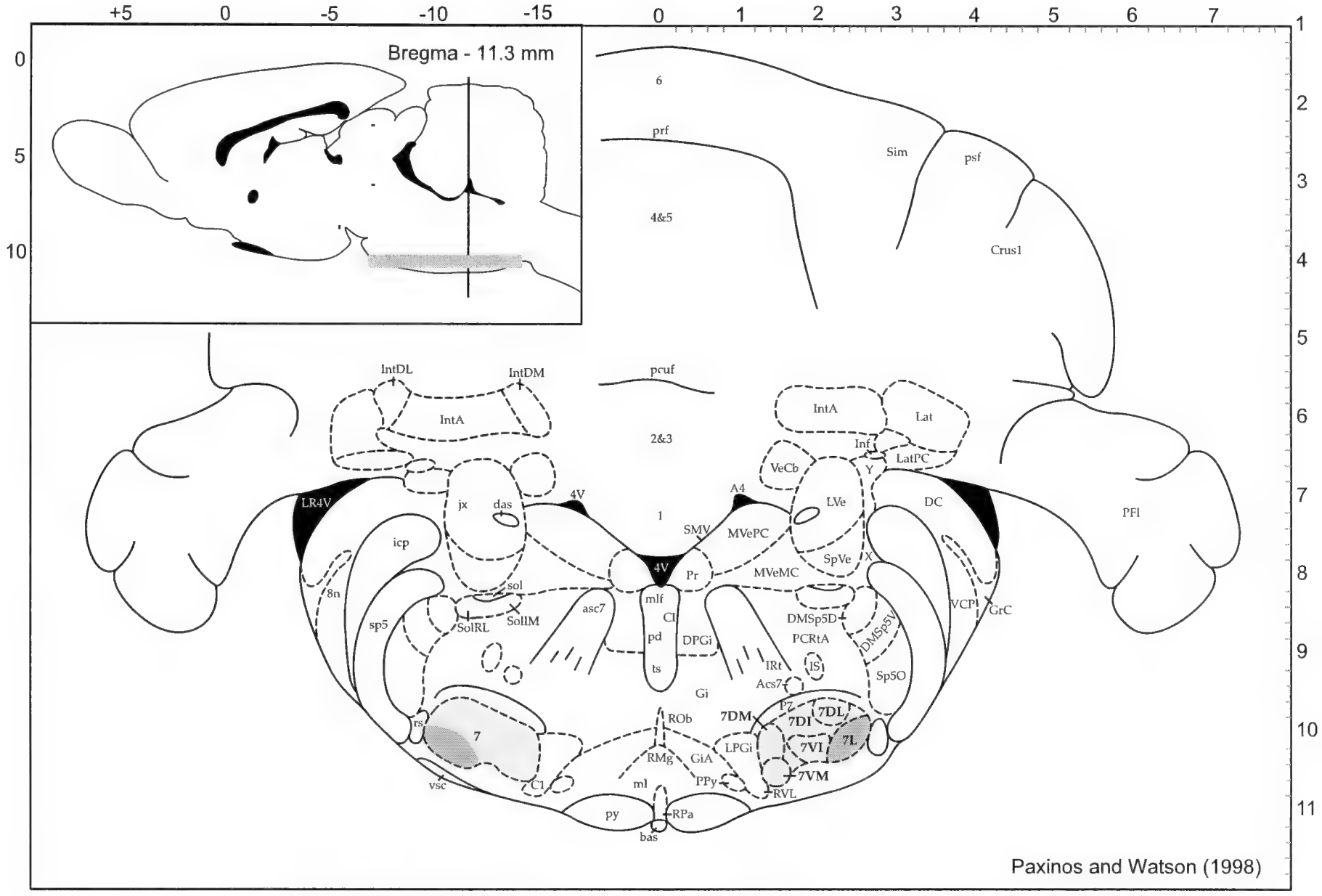
- Epidermal endings
- Upper dermal endings
- Circular follicle neck endings
- Penetrating follicle neck ending
- Circumferential free nerve endings
- Vascular endings

Art = arteriole
BM = Basement membrane
C = FSC capsule
CS = cavernous sinus
Ep = epidermis
F = follicle
GH = guard hair
ICB = inner conical body
IRS = inner root sheath
MS = mesenchymal sheath
ORS = outer root sheath
RS = ring sinus
RW = ringwulst
SG = sebacceous gland
UD = upper dermis
V = vibrissa
VH = vellus hair

Motor control in the vibrissa scanning sensorimotor system

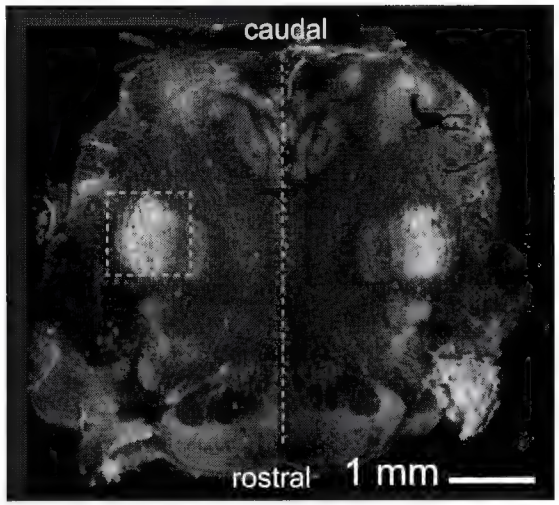
- Phenomenology of whisking
- **Anatomy and physiology of facial motoneurons**
- Multi-phasic and multi-level control of whisking
- Brainstem sensorimotor feedback

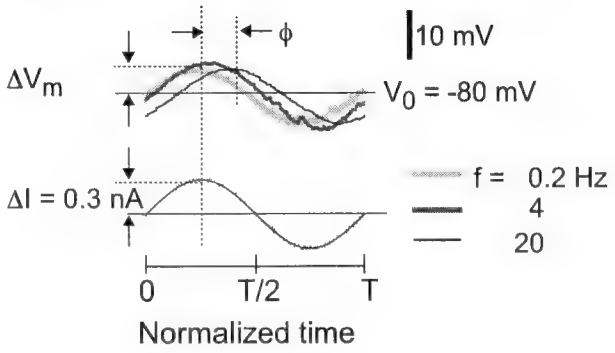
Motoneurons that drive the follicles are in the lateral facial (7L) nucleus (Klein and Rhoades 1985)

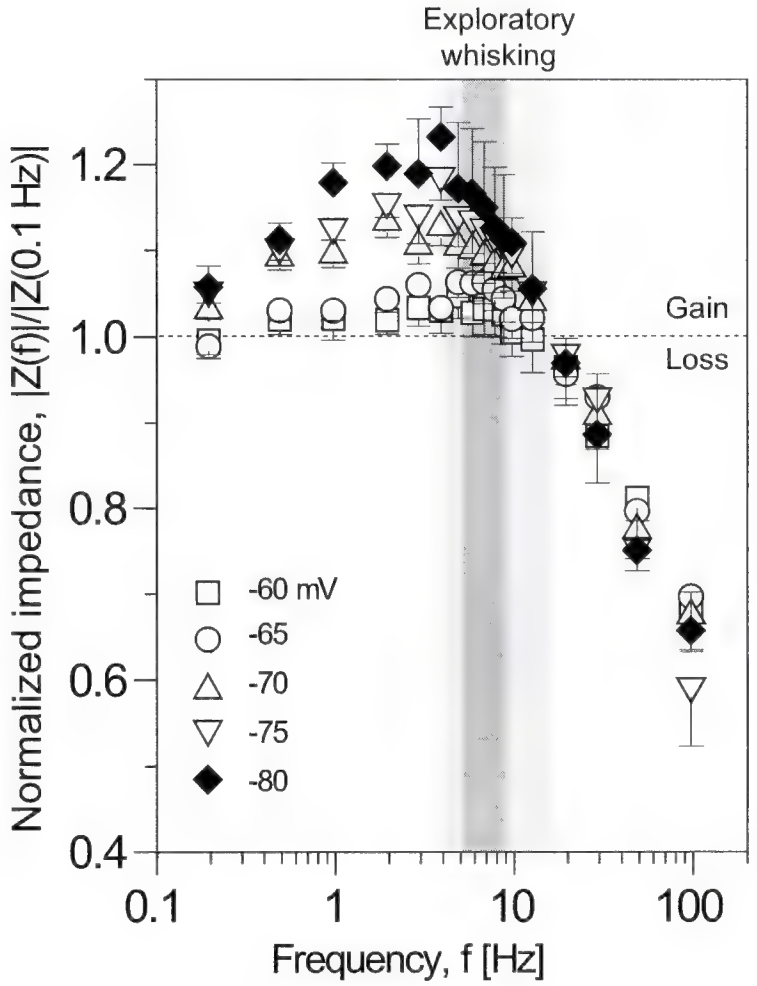


Paxinos and Watson (1998)

Subthreshold amplification in mature vibrissa motoneurons

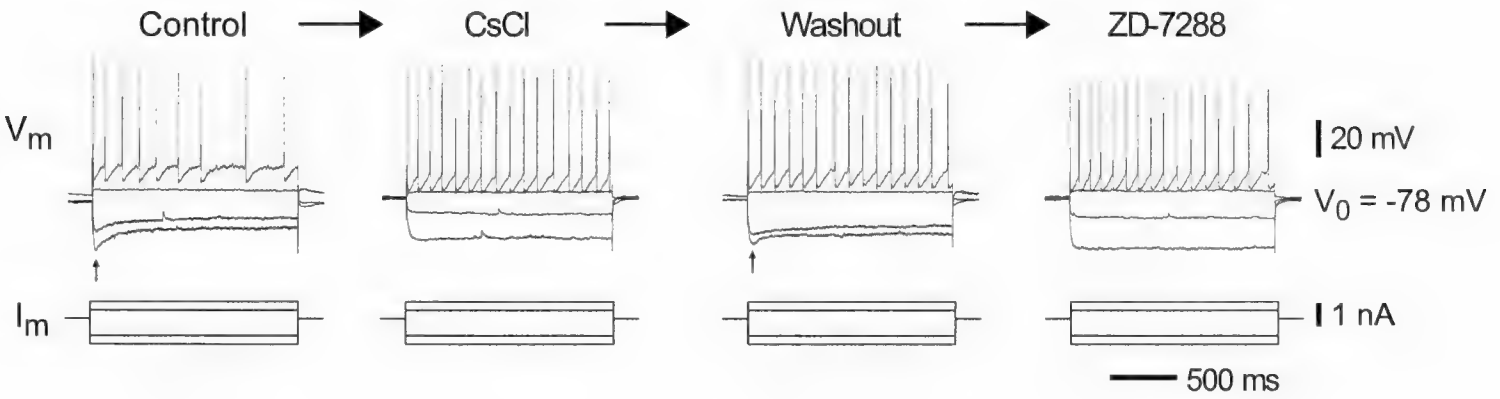


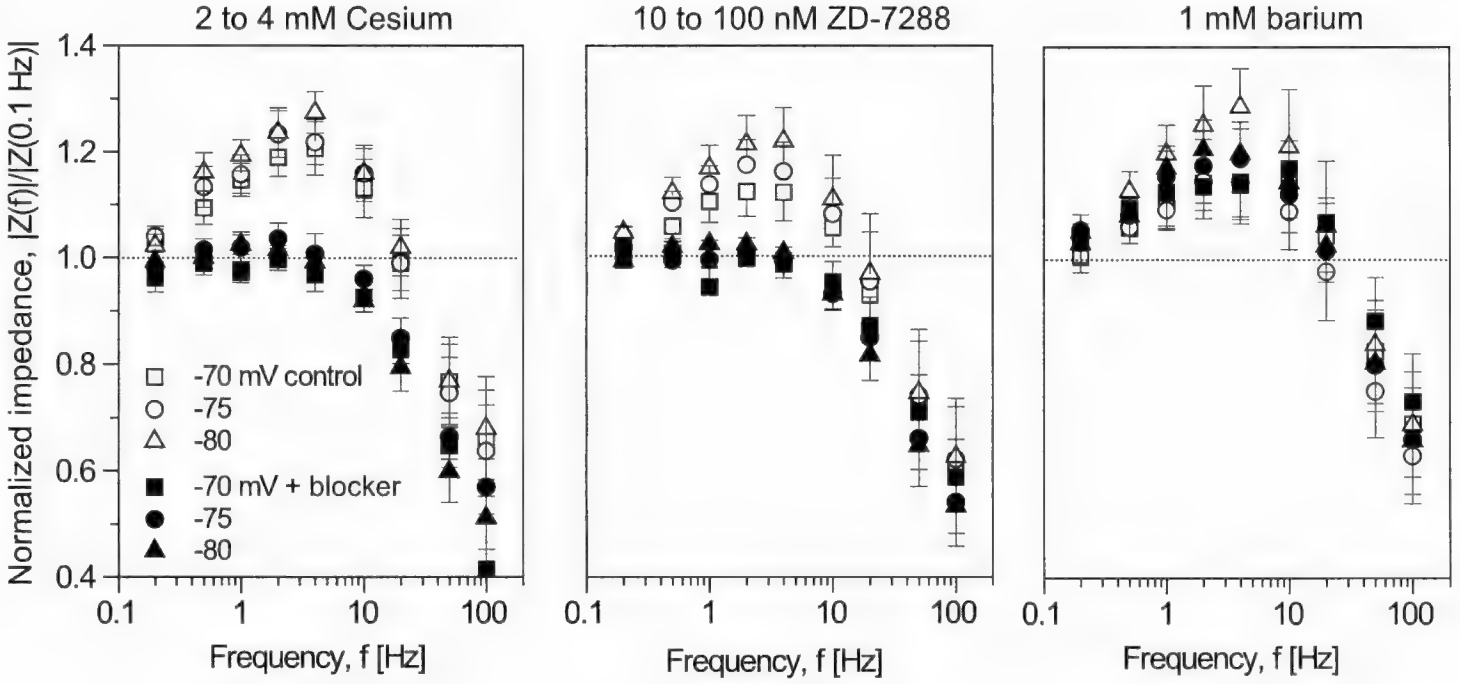




Nguyen, Wessel and Kleinfeld (2004)

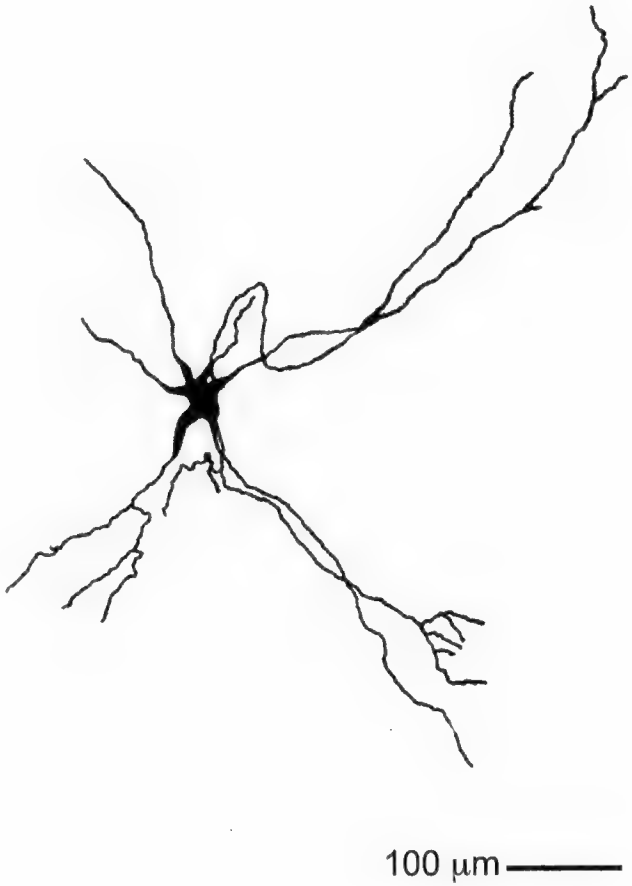
High-pass filtering in vibrissa motoneurons depends on I_h (hyperpolarization activated depolarizing current)

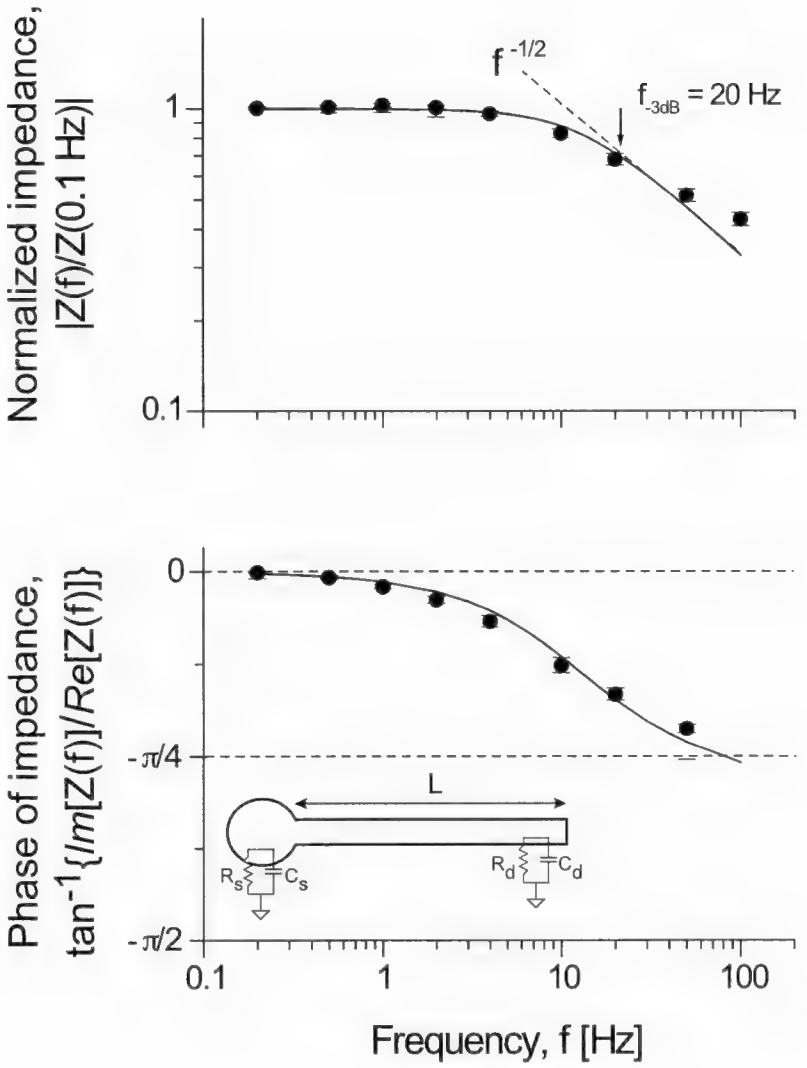




Nguyen, Wessel and Kleinfeld (2004)

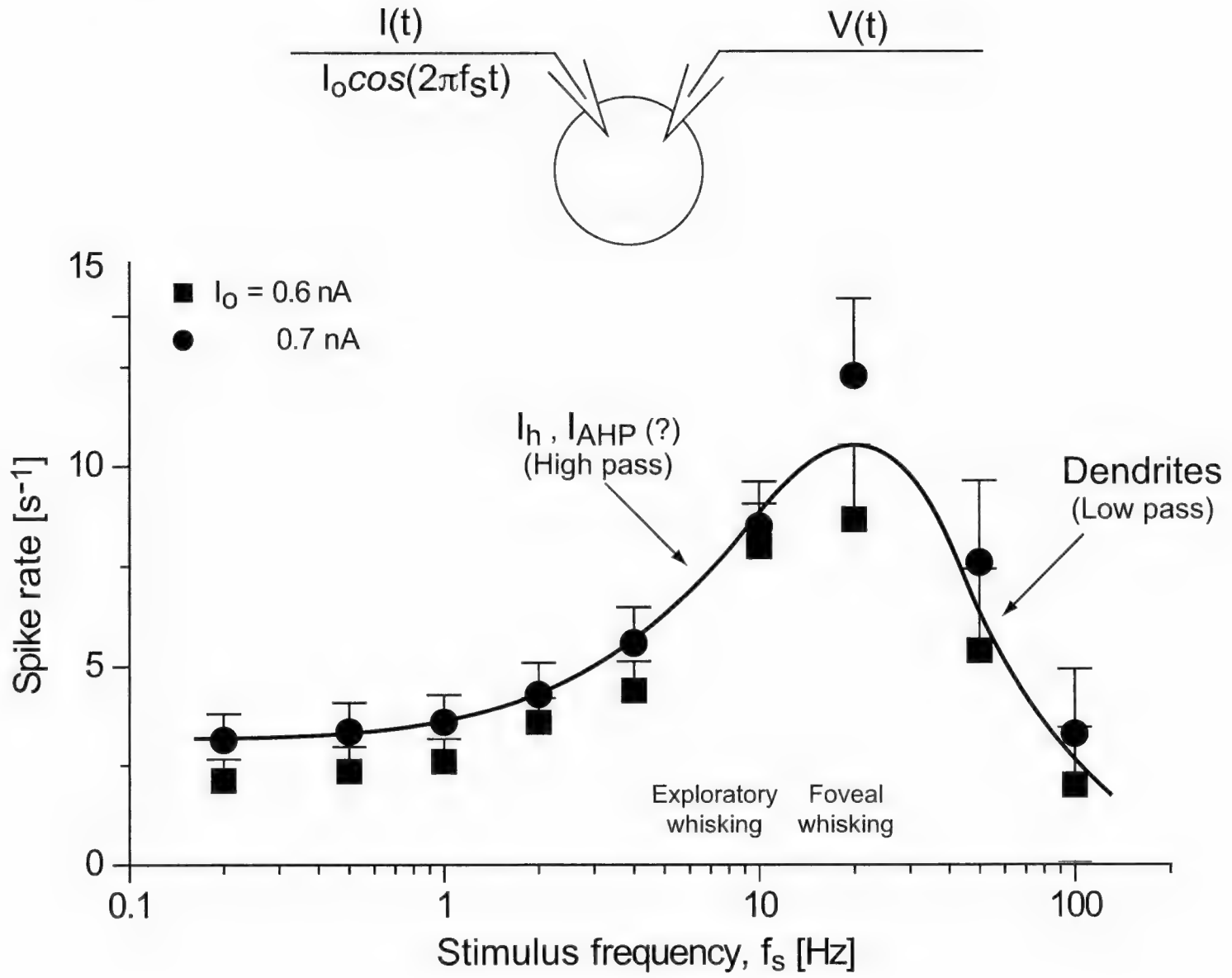
Low-pass filtering in vibrissa motoneurons is consistent with linear cable properties, *i.e.*, $Z(f) \sim 1/\sqrt{f}$ for $L >> \lambda$





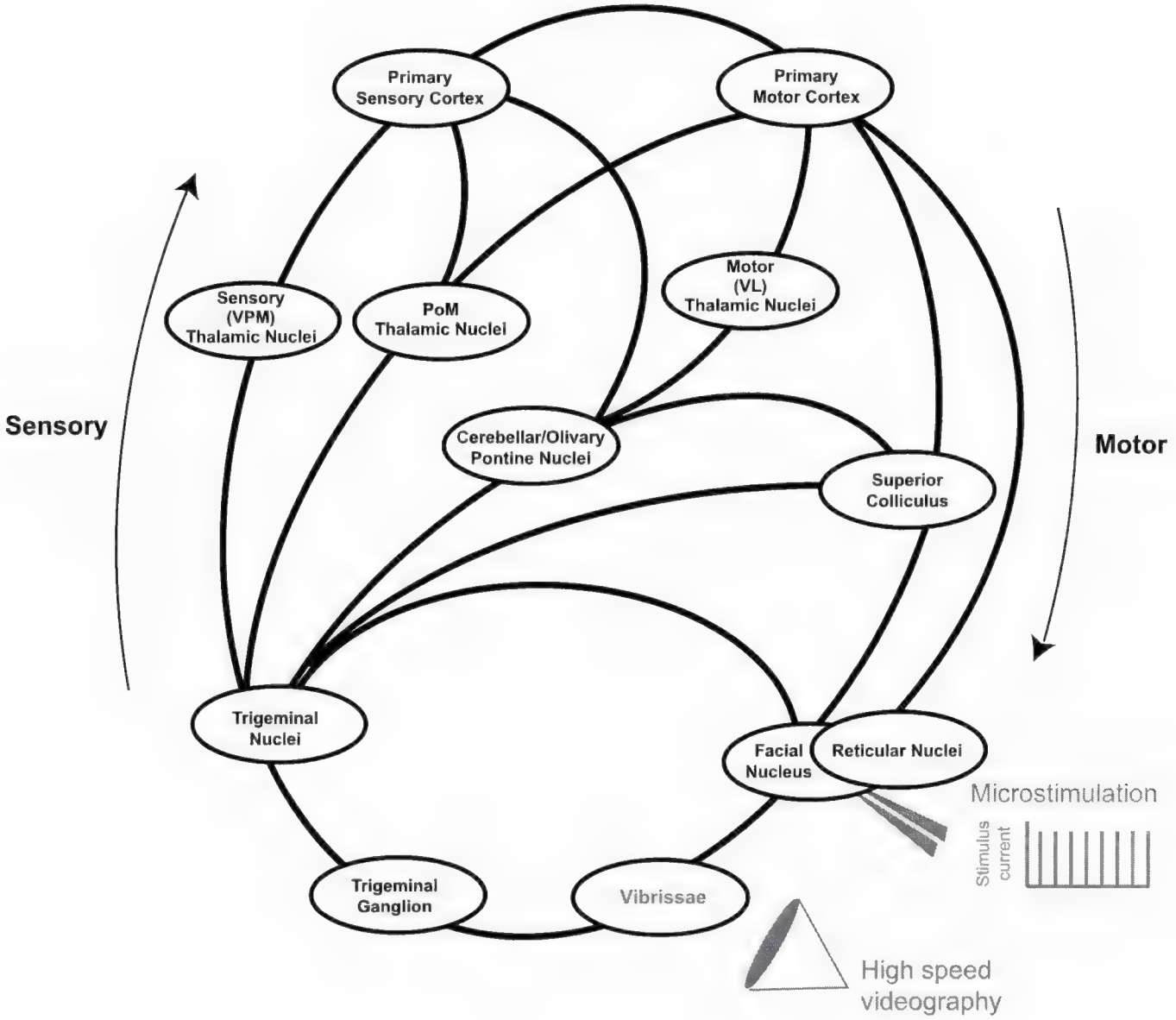
Nguyen, Wessel and Kleinfeld (2004)

Spiking resonance at whisking frequencies in vibrissa motoneurons

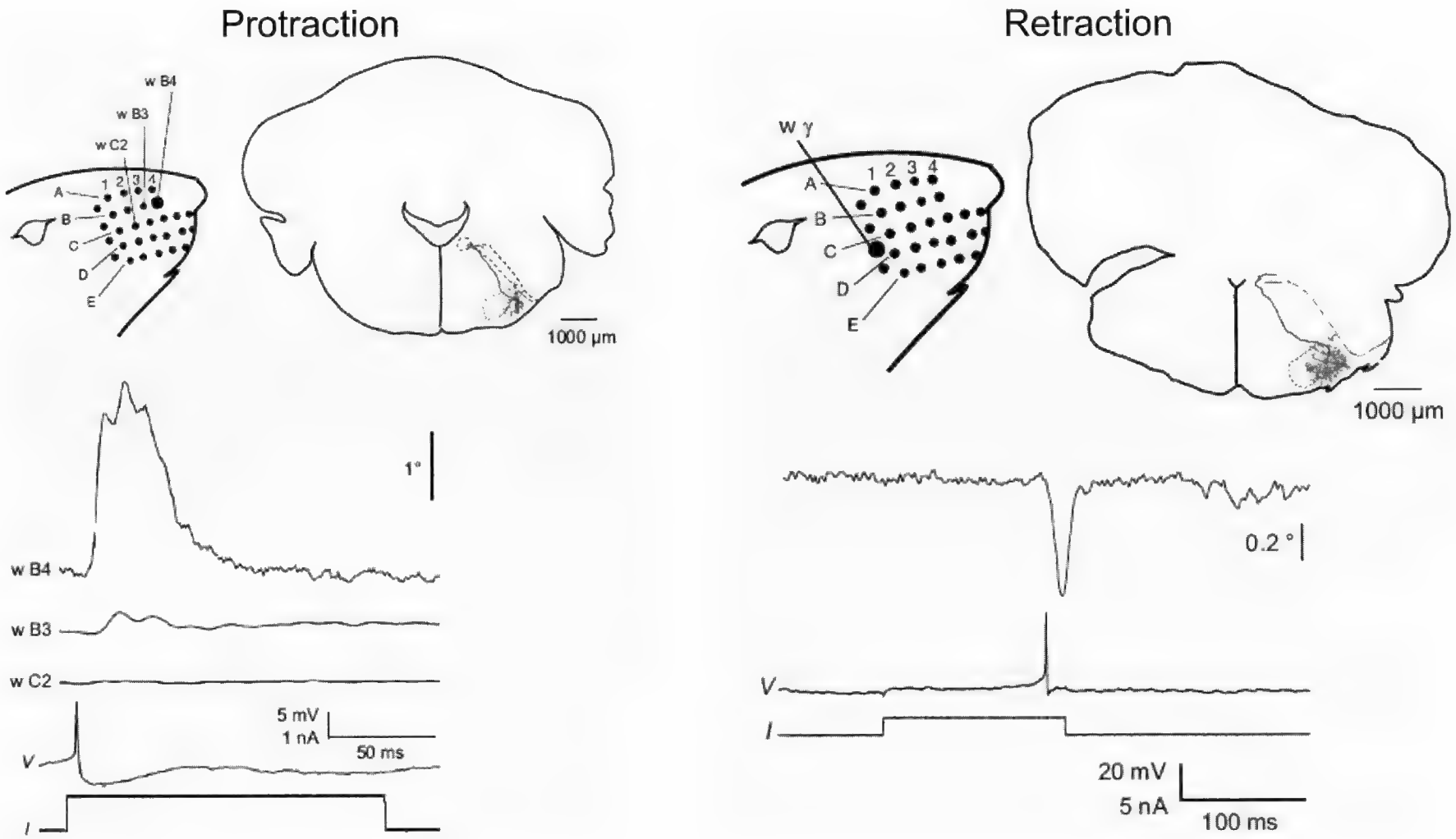


Nguyen, Wessel and Kleinfeld (2004)

Vibrissa motion in response to microstimulation of the facial nucleus (7V)



Microstimulation of individual motoneurons in facial nucleus (7V) leads to vibrissa movement (Herfst and Brecht 2008)



Lesson 2

Motoneurons have a resonance at whisking frequencies

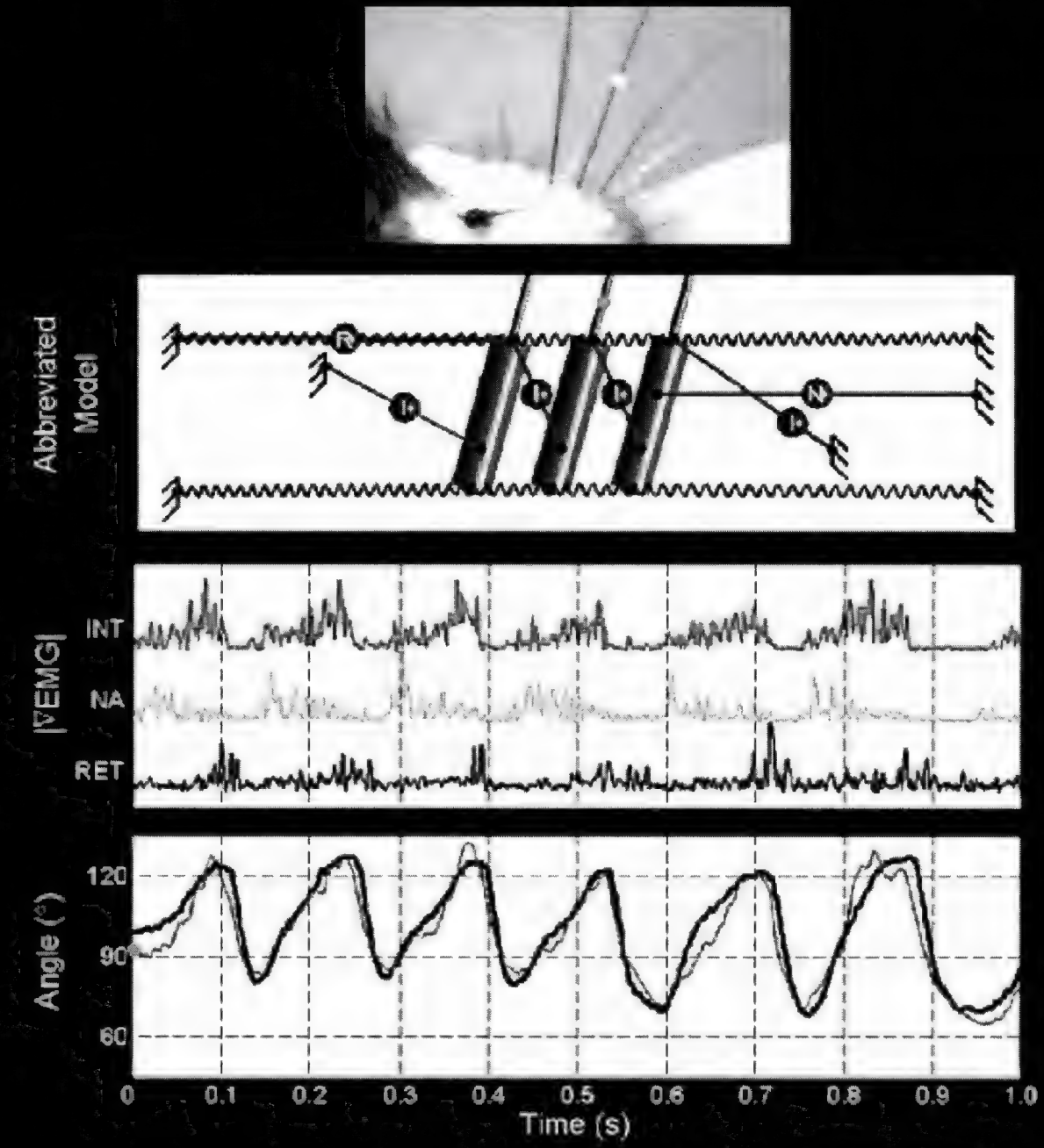
Individual motoneurons can drive the vibrissae

Query

Where is the pattern generator for whisking?

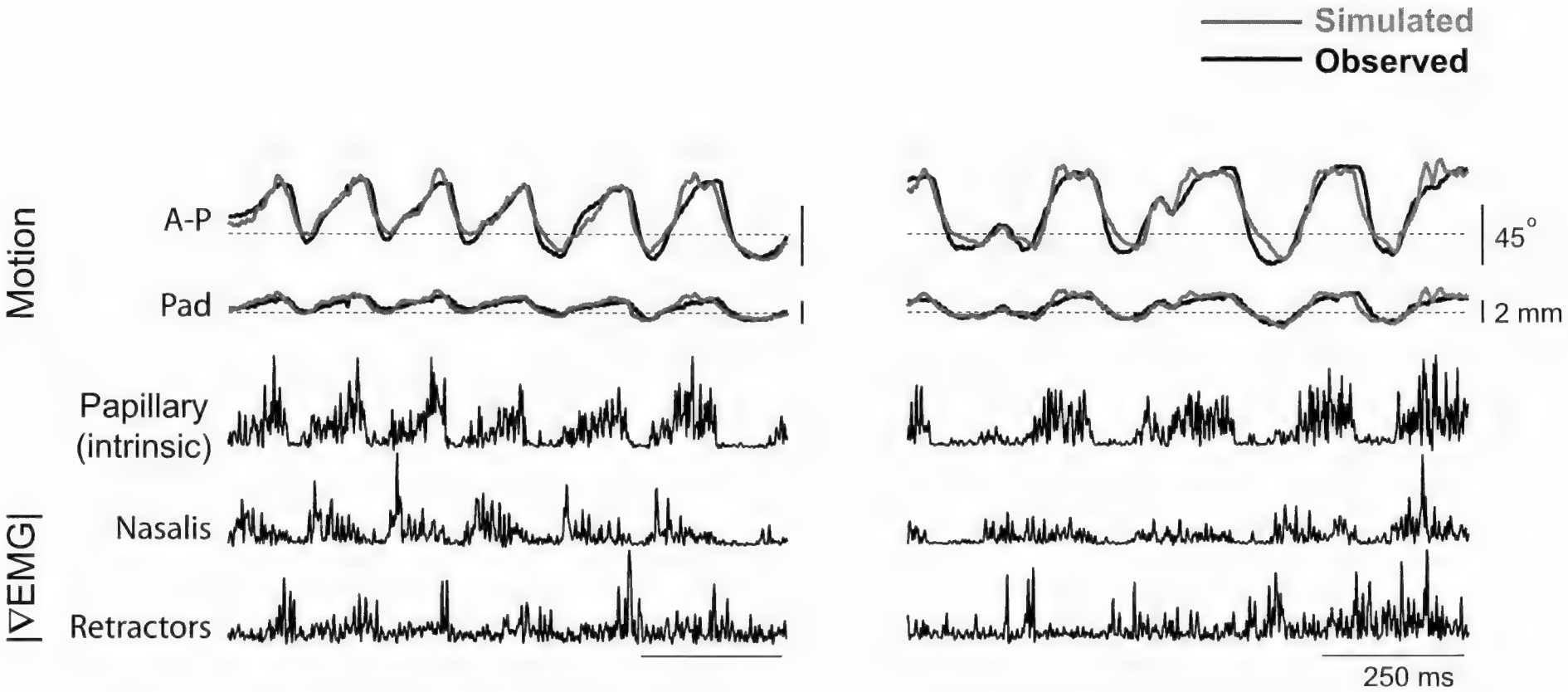
Motor control in the vibrissa scanning sensorimotor system

- Phenomenology of whisking
- Anatomy and physiology of facial motoneurons
- **Multi-phasic and multi-level control of whisking**
- Brainstem sensorimotor feedback



Hill, Bermejo, Zeigler and Kleinfeld (2008)

Measured vibrissa motion can be predicted from triphasic EMG activity



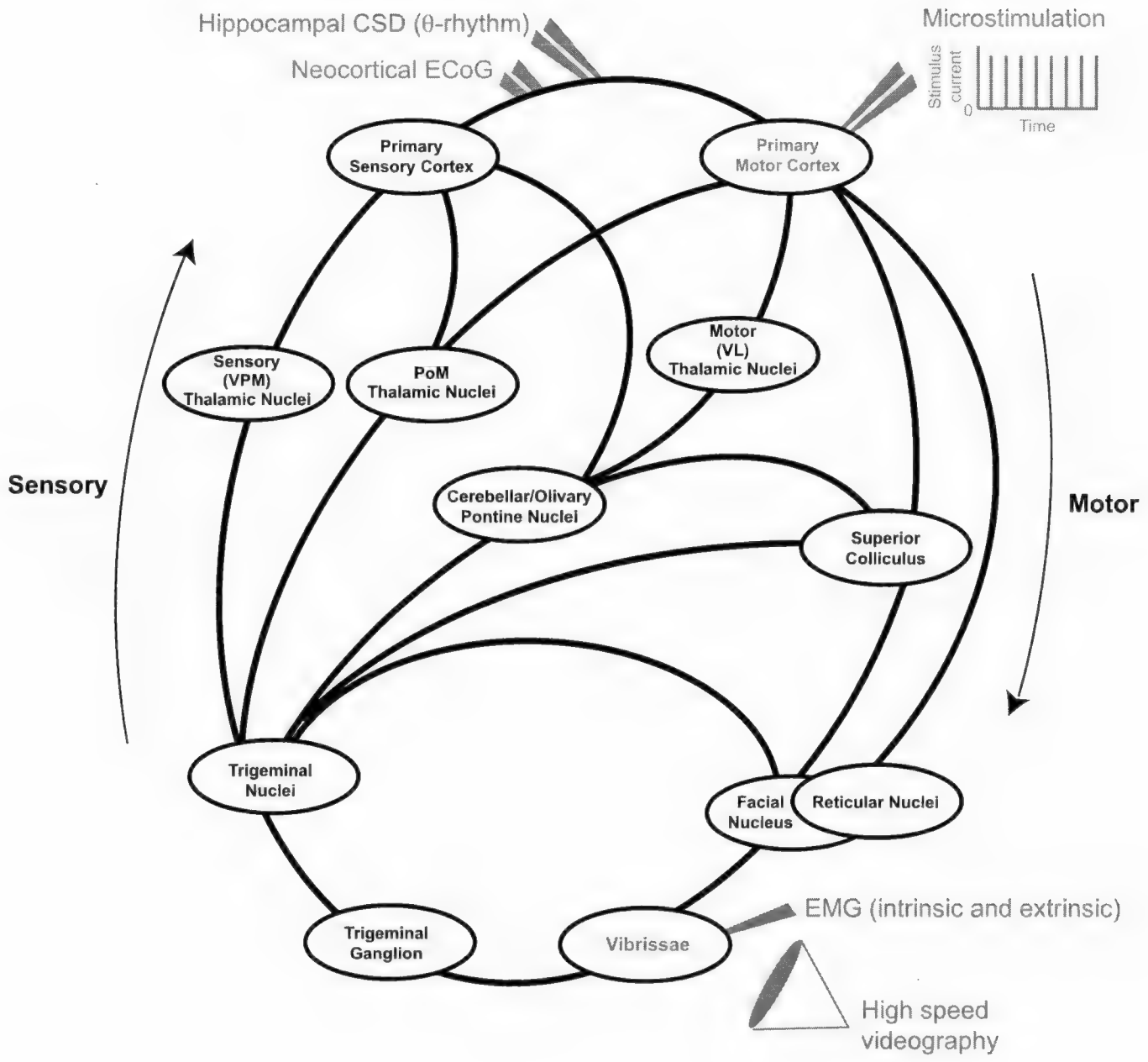
Validation on 100 whisks

Mean whisk amplitude = 64°

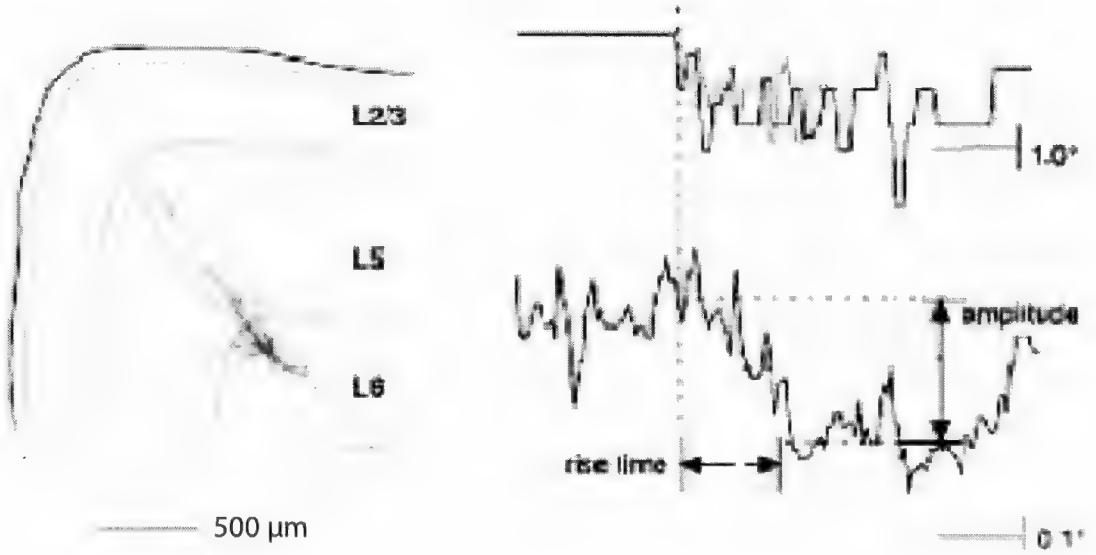
RMS prediction error = 7.8°

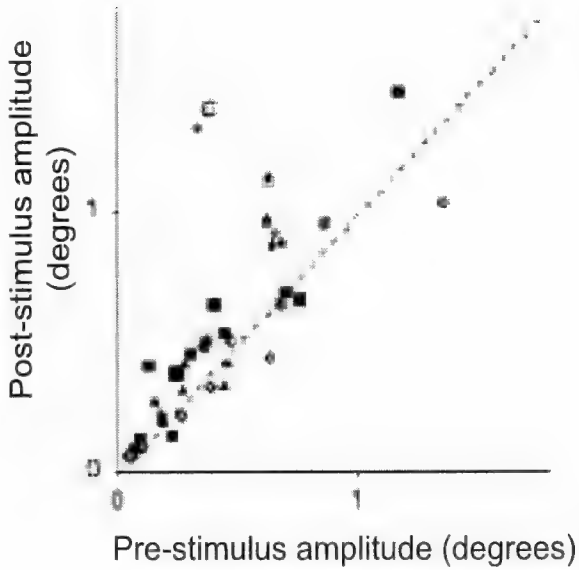
Hill, Bermejo, Zeigler and Kleinfeld (2008)

Vibrissa motion in response to periodic microstimulation of M1 cortex

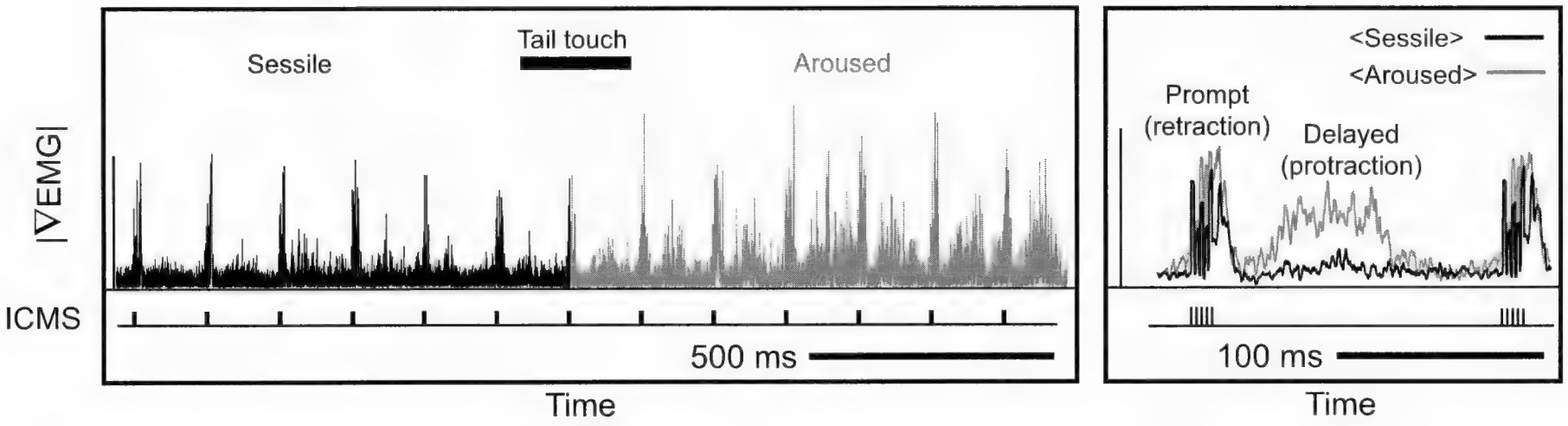


Single neurons in M1 cortex can drive movement of the vibrissae (Brecht, Schneider, Sakmann and Margrie, 2004)





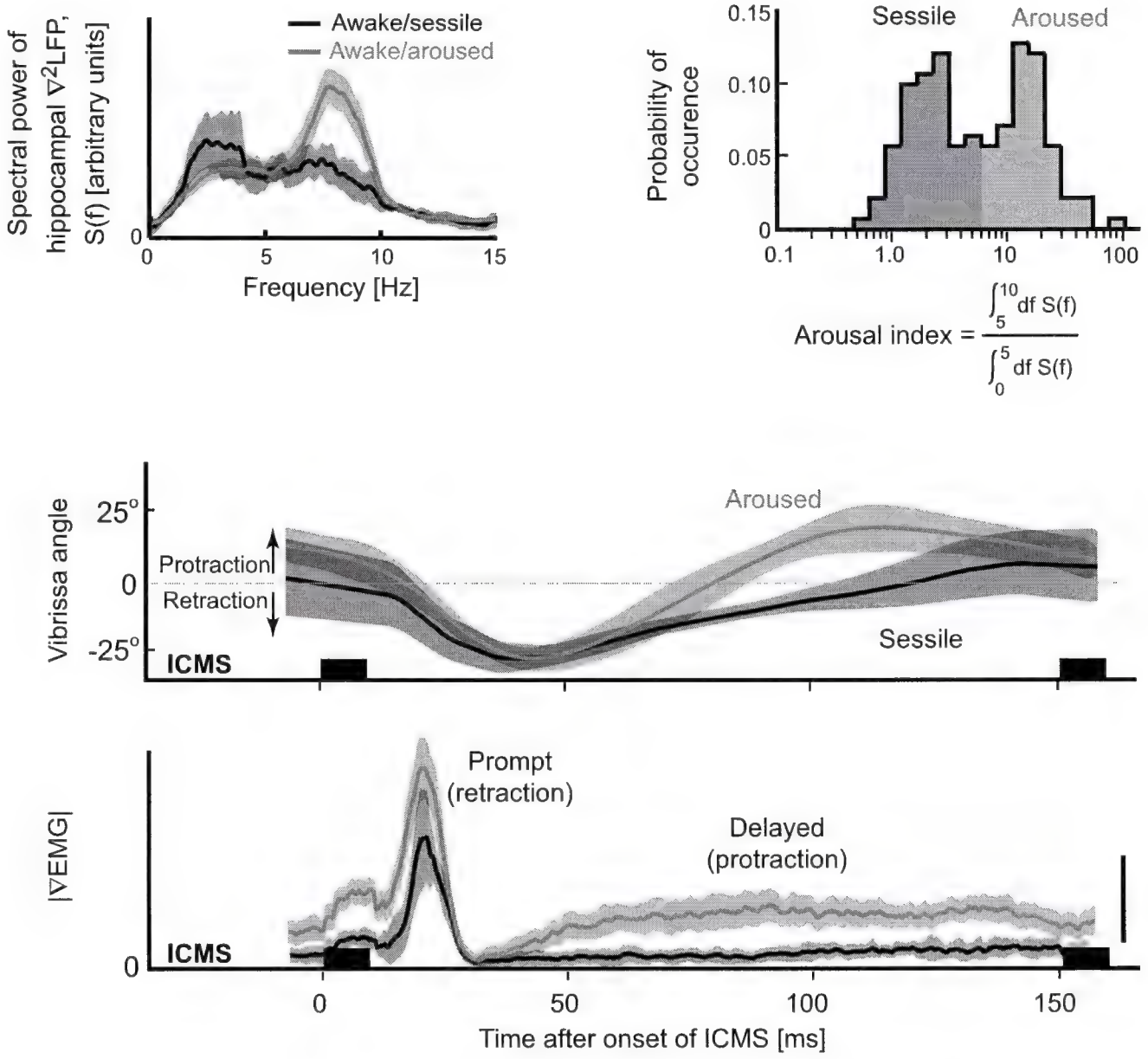
ICMS to vibrissa M1 cortex drives retraction in the sessile rat



Addition of function - protraction - through arousal

Berg and Kleinfeld (2003)

ICMS to M1: Normal pattern of whisking in the aroused, but not sessile, rat



Berg, Friedman, Schroeder and Kleinfeld (2005)

Lesson 3

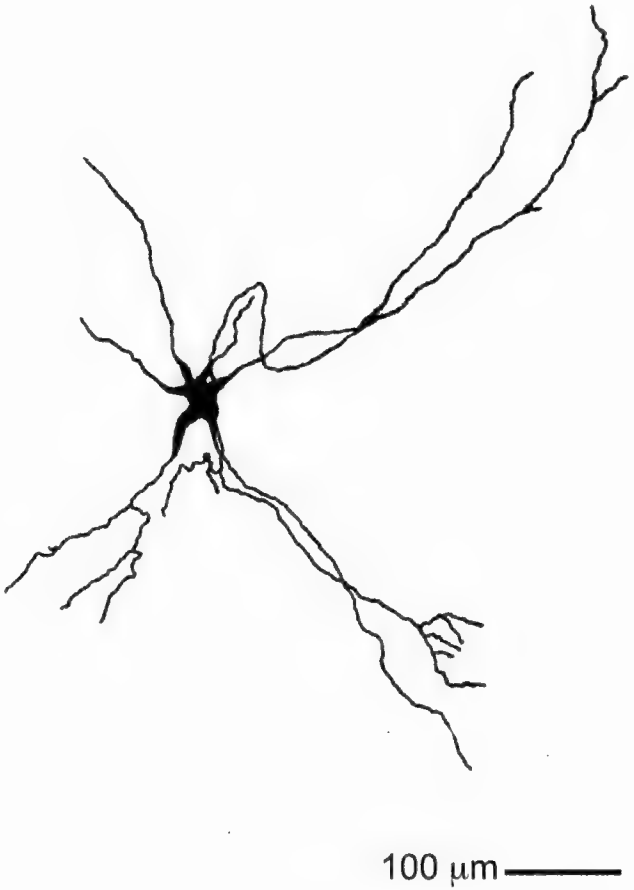
Whisking depends on a 3-phase (unidentified) pattern generator

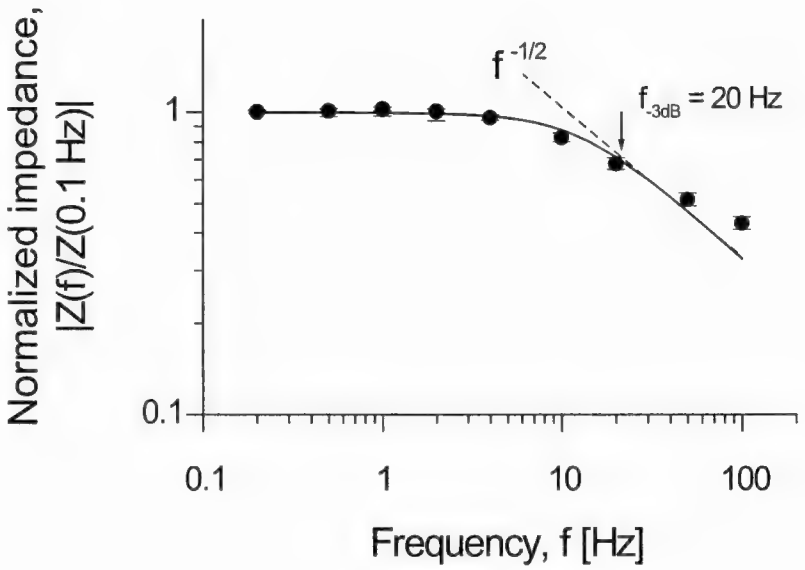
Cortex can drive whisking in real-time in the aroused (Ach ↑) state

Query

How are the multiple levels of control arbitrated?

Recall that the dendrites of vibrissa motoneurons are electrically long,
i.e., $Z(f) \sim 1/\sqrt{f}$ for $L >> \lambda$

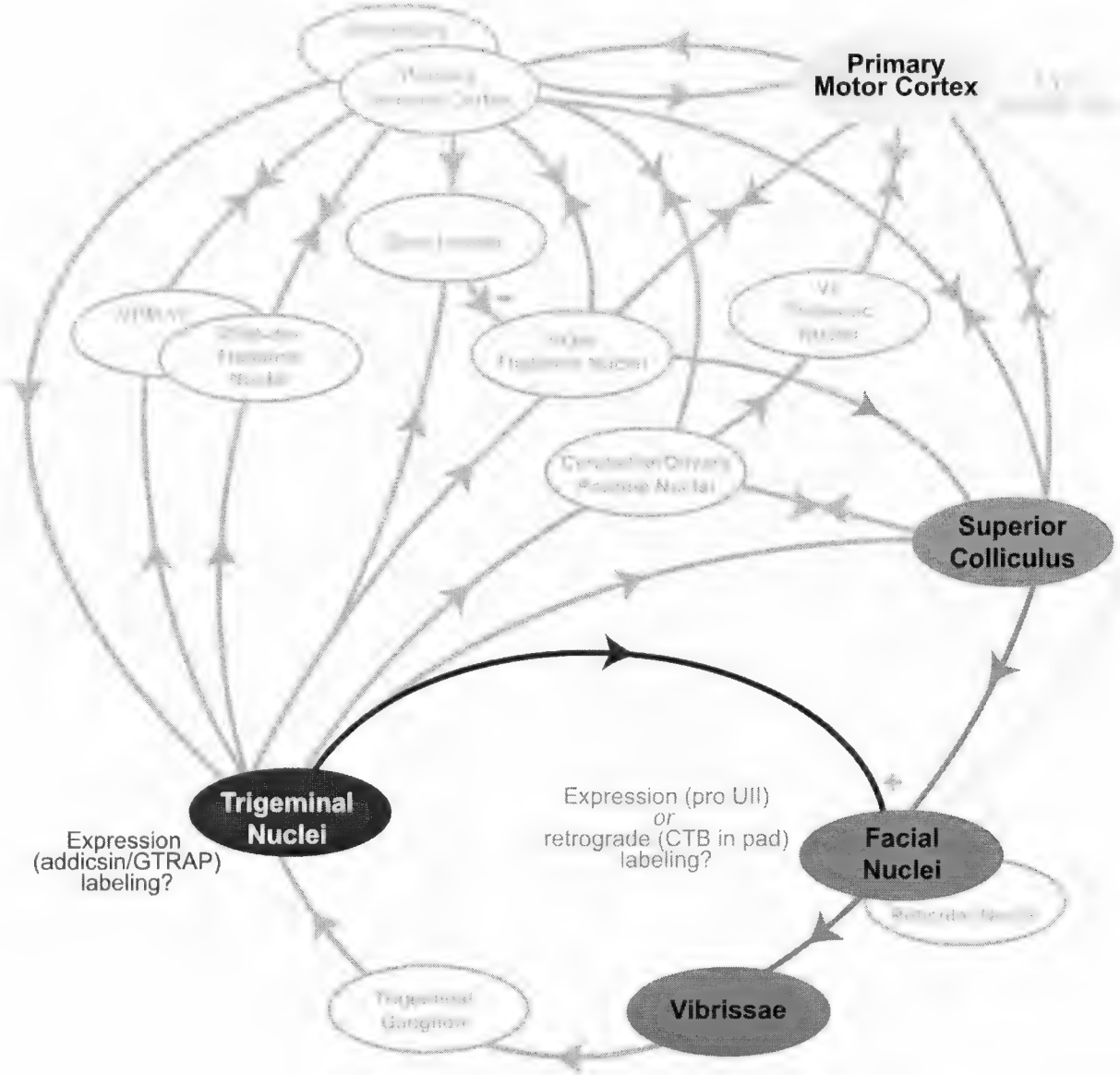




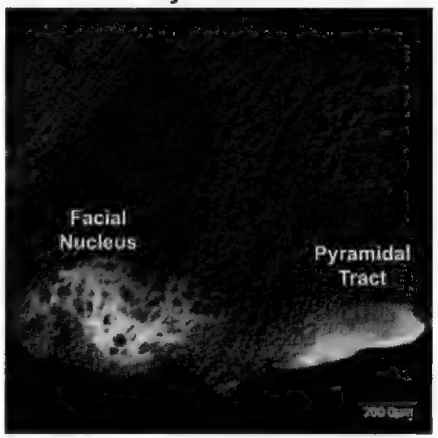
Implies that dendritic inputs may functionally segregate

Nguyen, Wessel and Kleinfeld (2004)

Approach to study feedback to vibrissa motoneurons in facial nuclei by analogy with CRACM (Petreanu, Huber, Sobczyk and Svoboda, 2007)



M1 cortex to FN projections in a Thy1 mosaic line

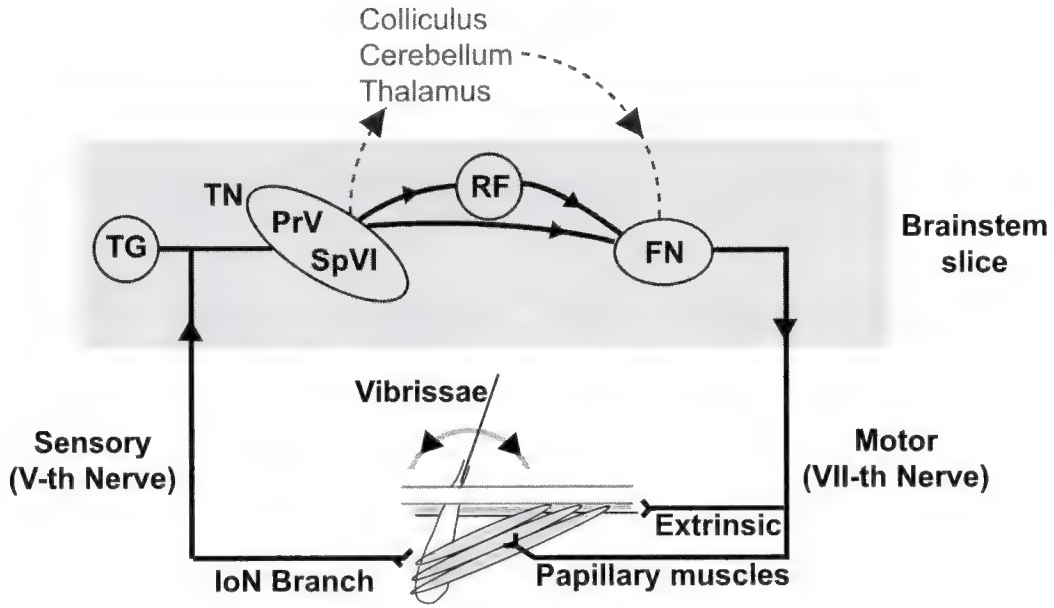


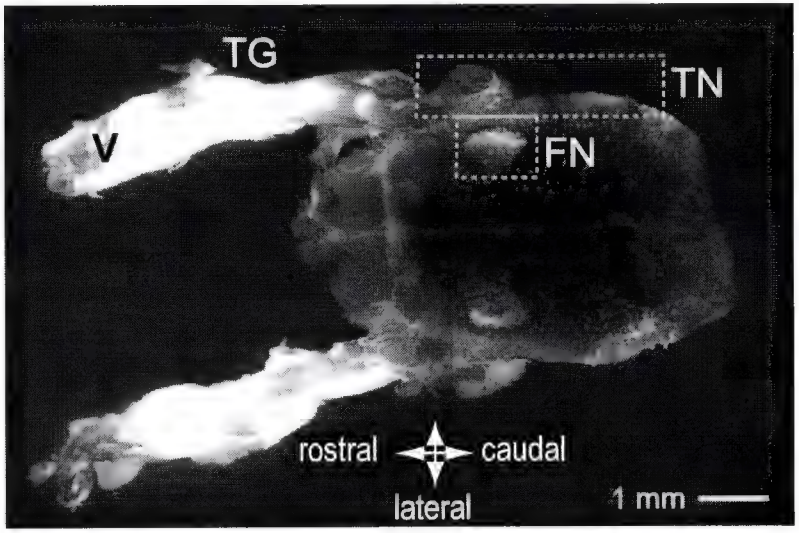
(convergence of 40 inputs from pons, medula, midbrain, and hindbrain, half with M1 afferents)

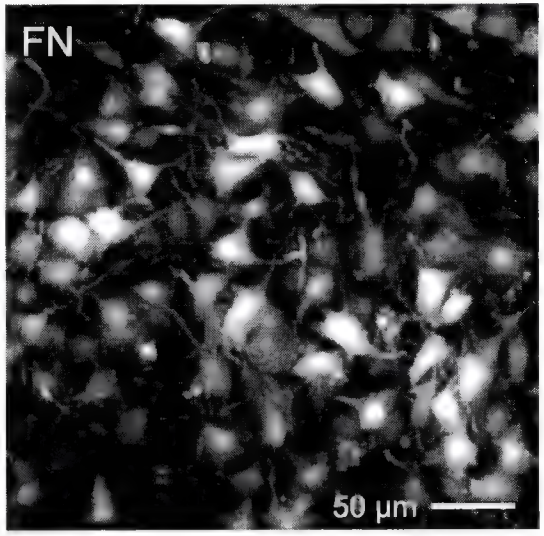
Motor control in the vibrissa scanning sensorimotor system

- Phenomenology of whisking
- Anatomy and physiology of facial motoneurons
- Multi-phasic and multi-level control of whisking
- **Brainstem sensorimotor feedback**

Brainstem slice preparation captures sensorimotor feedback circuitry

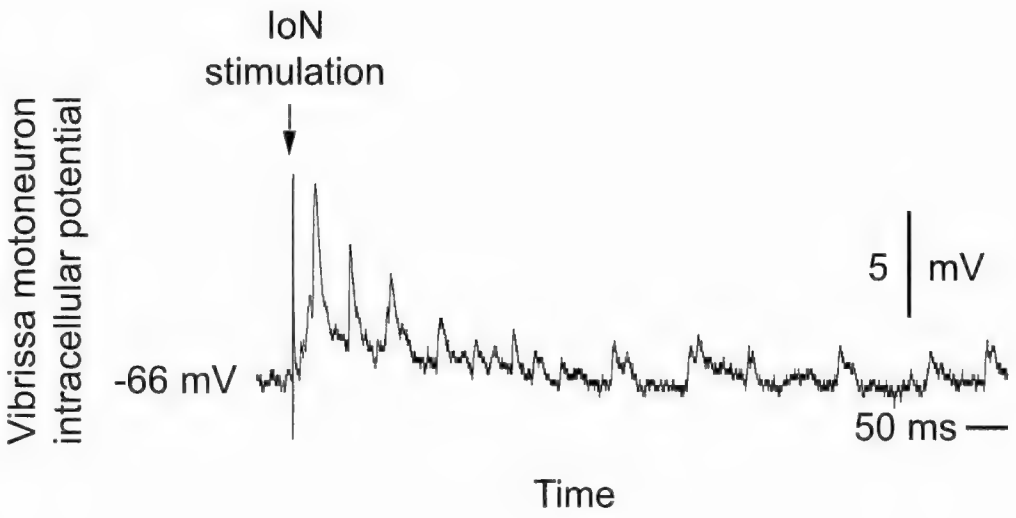


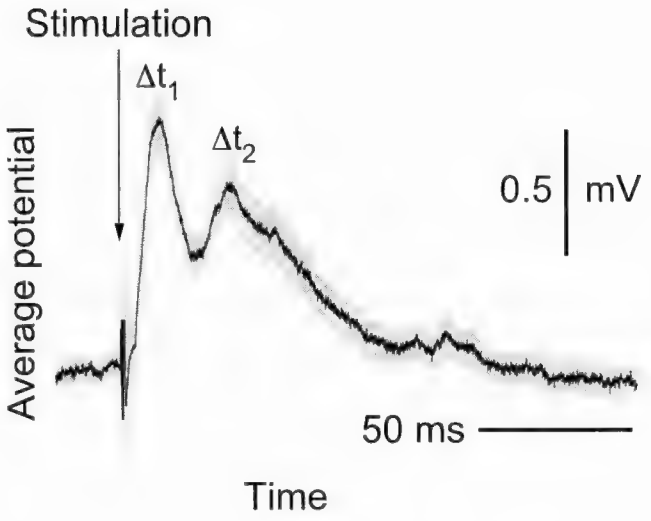




Nguyen and Kleinfeld (2005)

Fast, transient, positive feedback in the brainstem vibrissa sensorimotor loop *in vitro*

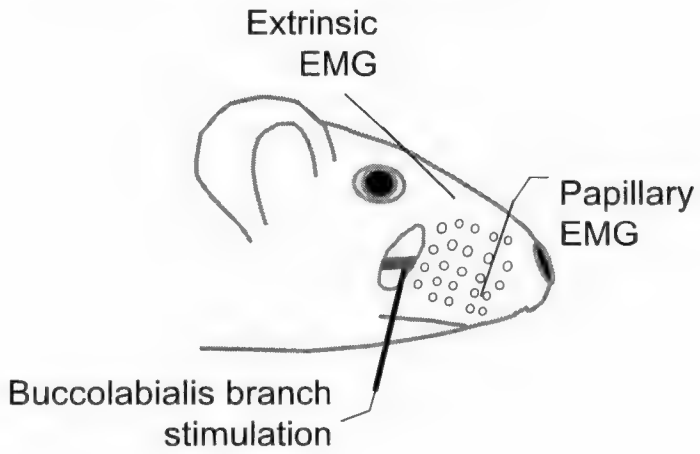




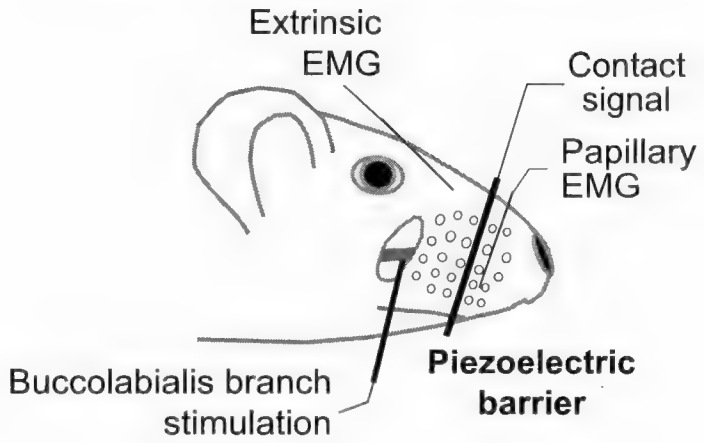
Nguyen and Kleinfeld (2005)

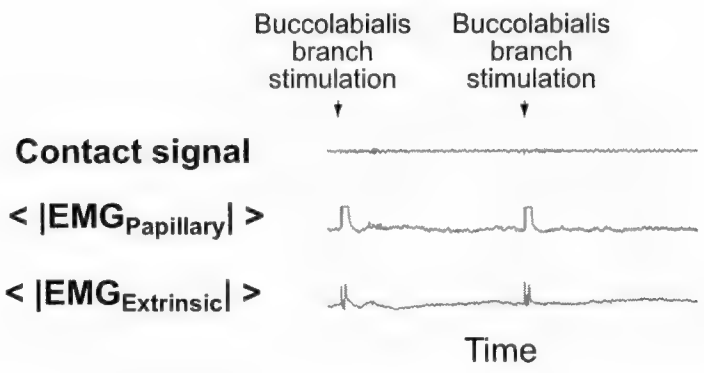
Fast, transient, positive feedback in the brainstem vibrissa sensorimotor loop *in vivo*

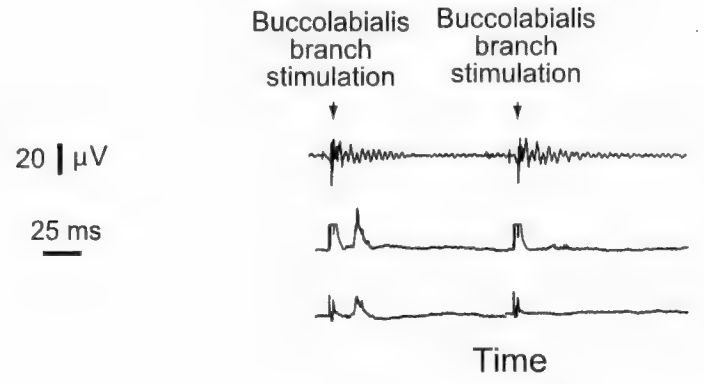
Control: Artificial whisking



Contact: Artificial whisking + barrier





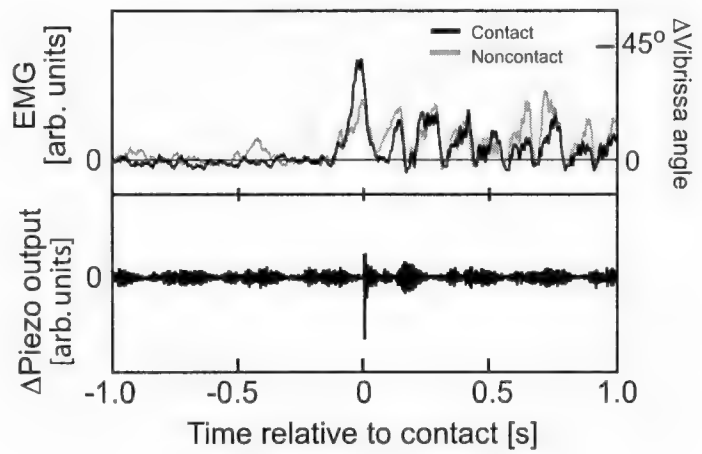


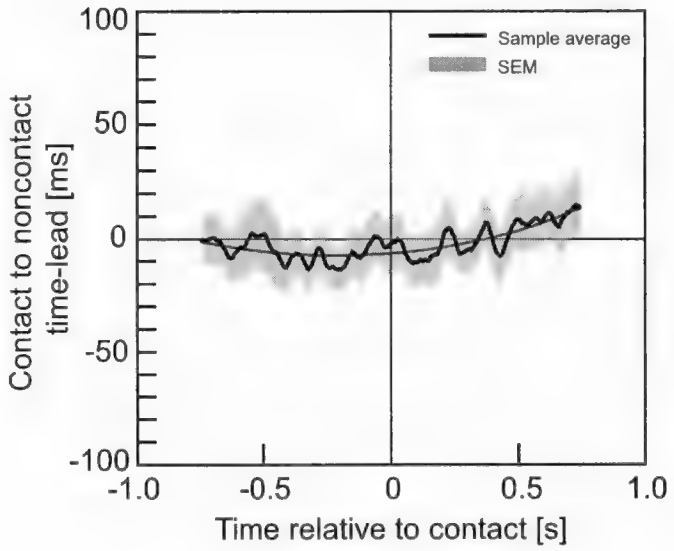
Nguyen and Kleinfeld (2005)

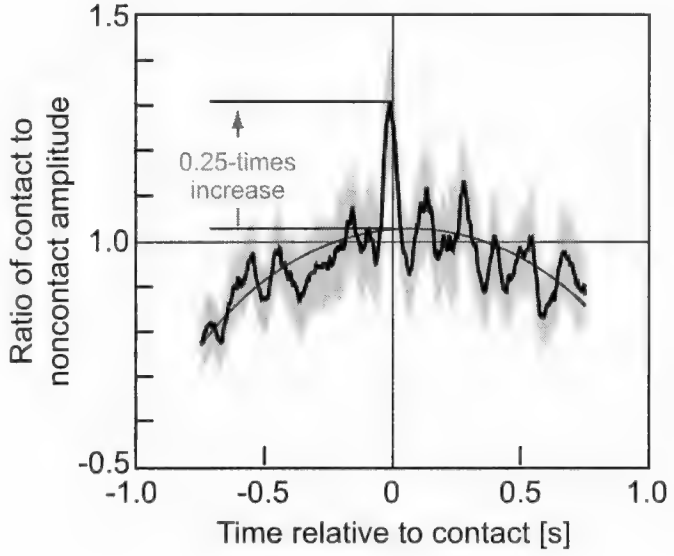
Rats can detect contact to a single vibrissa (Hutson and Masterson 1986)

Sachdev, Berg, Champney, Kleinfeld and Ebner (2003)

Vibrissa contact leads to transient increase in EMG during contact task (force ~ EMG)







Sachdev, Berg, Champney, Kleinfeld and Ebner (2003)

Lesson 4

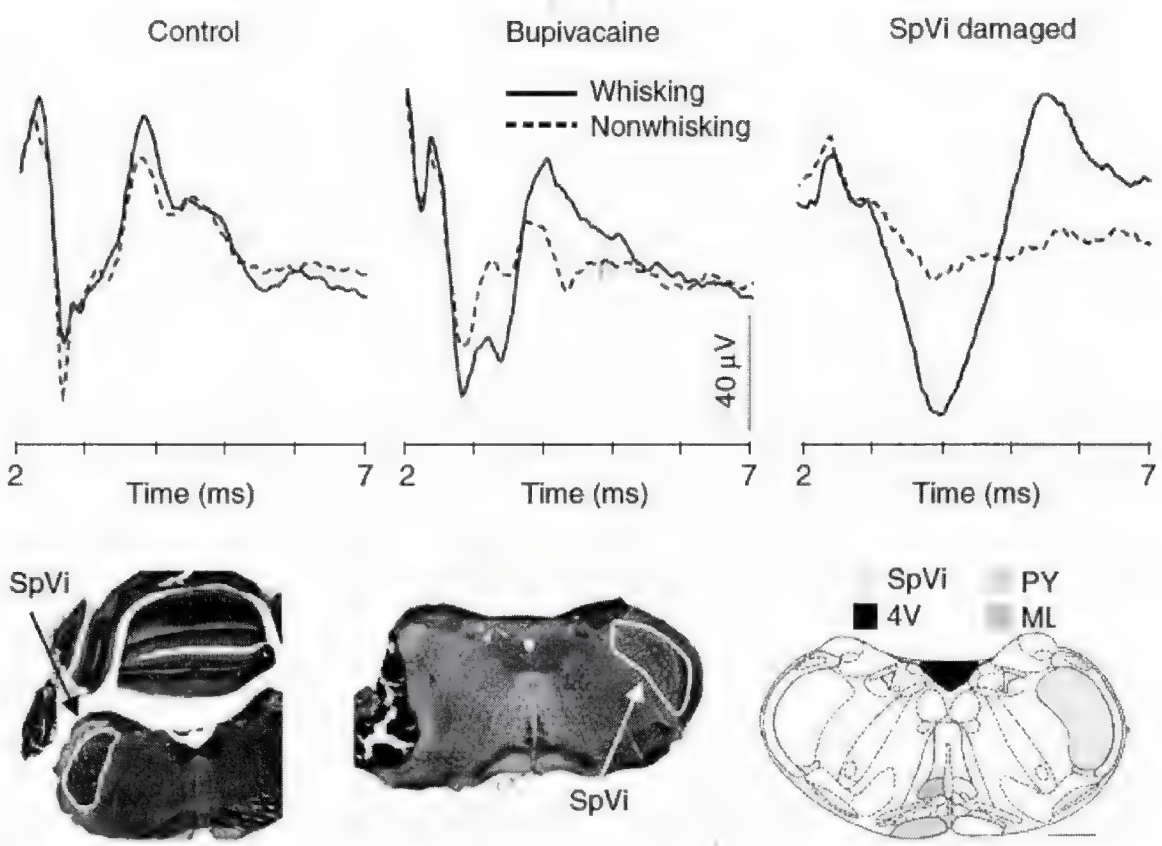
Sensory input provides positive feedback for heightened touch

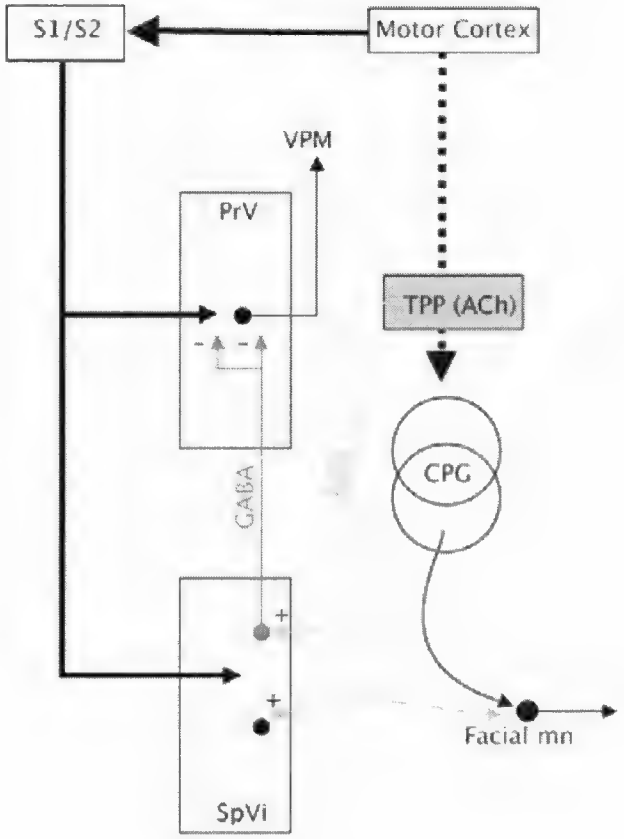
Sensory feedback plays a minor role in frequency modulation

Query

How is sensory input filtered at the level of the brainstem?

Potentially contradictory evidence that whisking gates sensory input



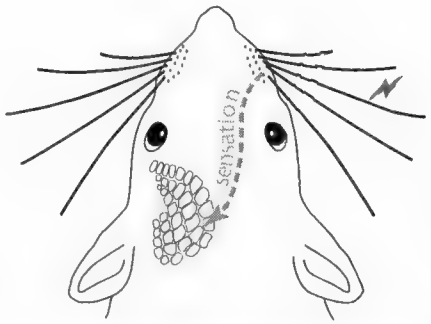


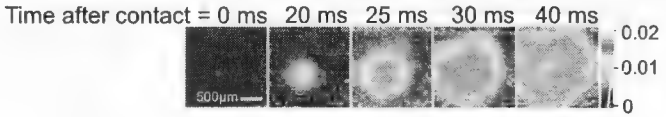
Thalamic response to follicle stimulation is enhanced by whisking (Lee, Carvell and Simons, 2008).

Response is further enhanced by block of SpVi, which normally gates PrV to “close” the feedforward pathway (Furuta, Timofeeva, Nakamura, Okamoto-Furuta, Togo, Kaneko and Deschênes, 2008)..

Potentially contradictory evidence that whisking gates sensory input

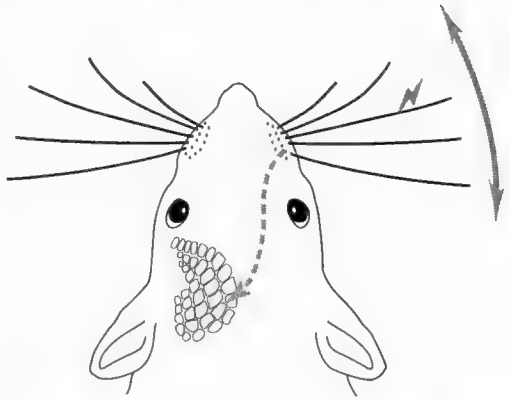
Startle mode (awake and sessile)

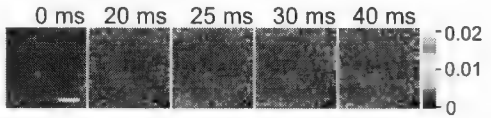




Strong response to passive stimulation

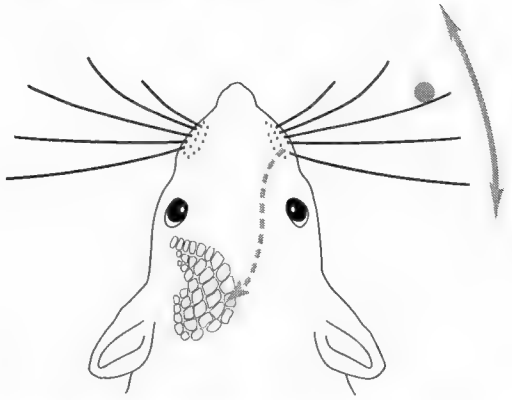
Exploration mode (whisking *without* contact)

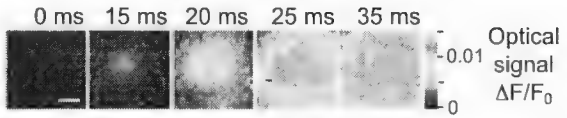




Gating or suppression yields *weak* response to passive stimulation

Object detection mode (whisking *with* contact)





Strong response to active touch

Suppression of cortical response during whisking without contact (Ferezou, Bolea and Petersen, 2006)

Summary

Motoneurons integrate efferents from brainstem through cortex.

Motoneurons insure that whisking is smooth.

Big questions

How is integration/arbitration of different inputs achieved?

What is the form and location of the putative 3-phase whisking CPG?

The brainstem loop in the vibrissa scanning sensorimotor system

Thank you for your attention

Coding object location in the vibrissa scanning sensorimotor system

David Kleinfeld, UCSD

MBL August 2009
Methods in Computational Neuroscience

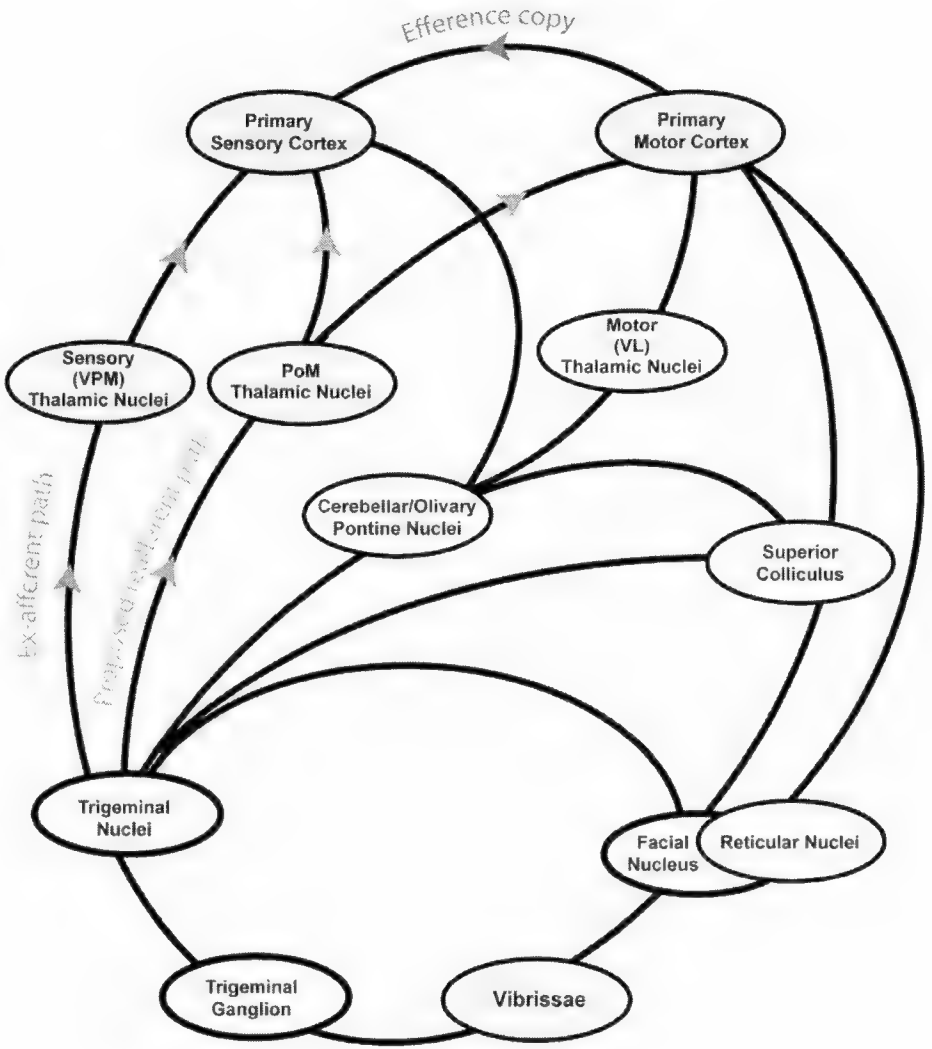
Nomenclature of sensorimotor signals
(von Helmholtz, ca. 1850; von Holst, 1954)

Ex-afference - originates from environmental influences, *e.g.*, pressure for the case of touching.

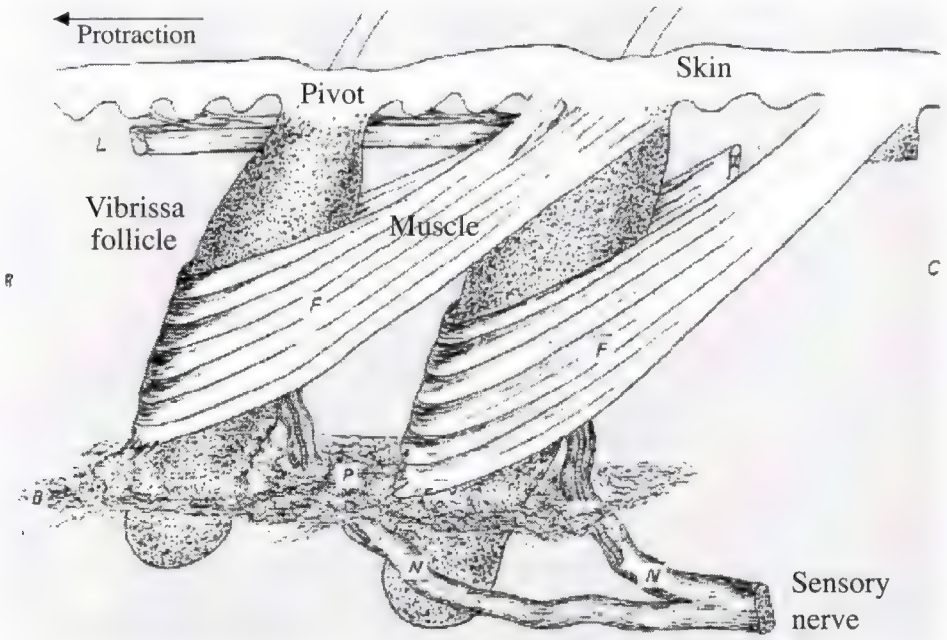
Reafference - originates from motor activation of sensory receptors.
Peripheral reafference - same receptors encode motor activation and external stimuli.
Proprioception - separate group of receptors encode motor activation.

Efference – brain commands to the motor plant.
Efference copy – corresponds to intended rather than actual motor activation of sensory receptors.

Ex-afference, reafference, and efference copy in the vibrissa system

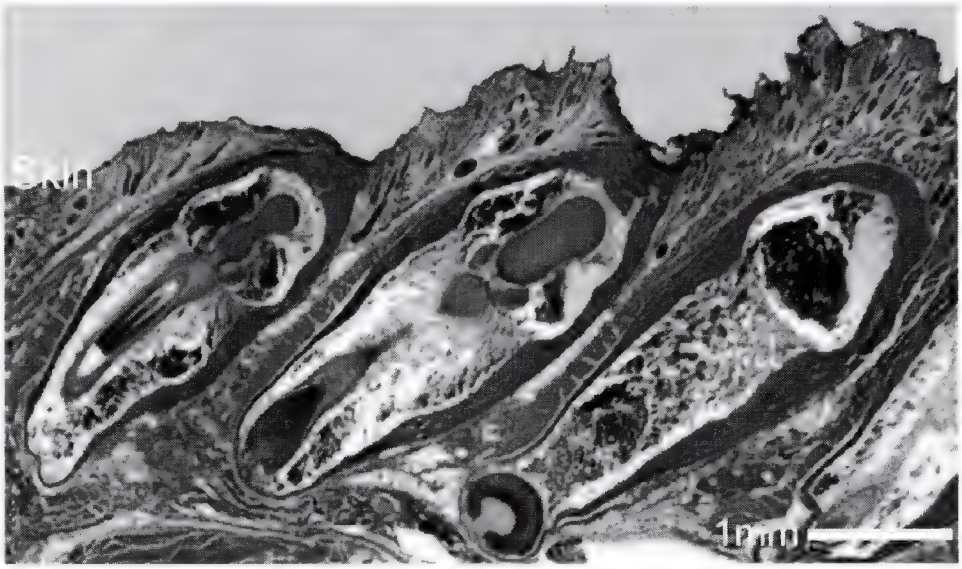


Papillary (intrinsic) muscles propel the follicles



Dorfl (1982)

Follicles abut each other



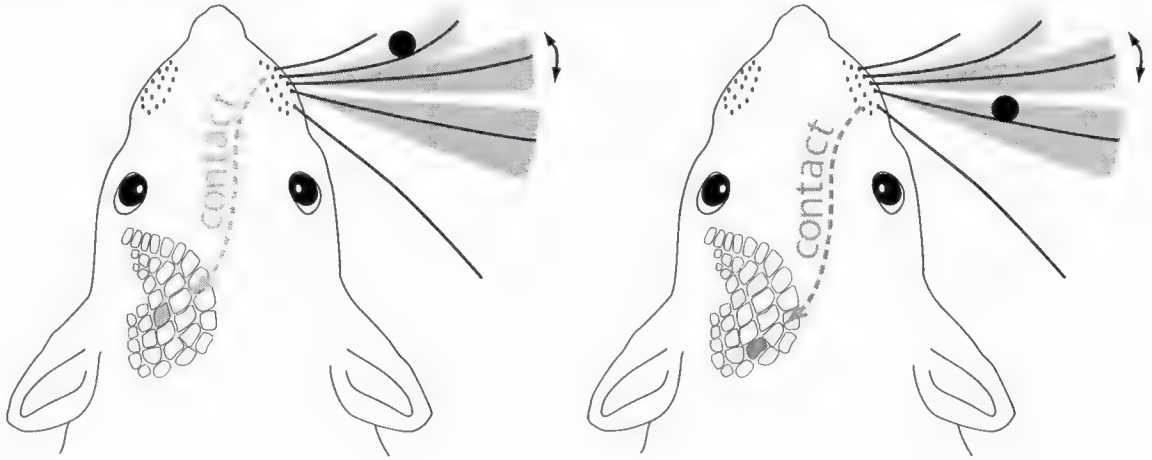
Hill, Bermejo, Zeigler, Kleinfeld (2008)

Coding object location in the vibrissa scanning sensorimotor system

- **Psychophysics of localization**
- Neurological basis of position signals
- Neurological basis of position dependent touch signals
- Coordinate representation in sensory (S1) versus motor (M1) areas

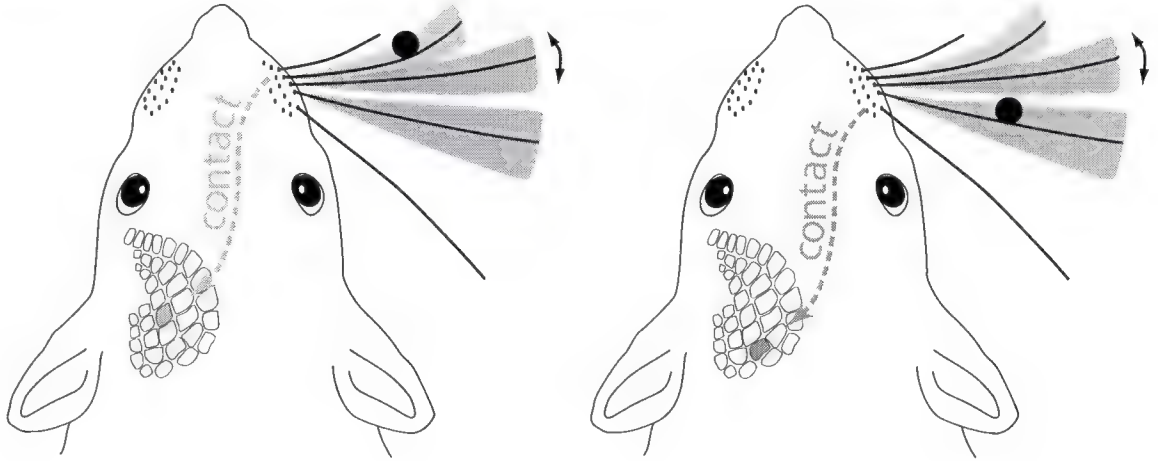
What class of algorithms are used to decode object location?

Labeled line and triangulation schemes: Require multiple vibrissae

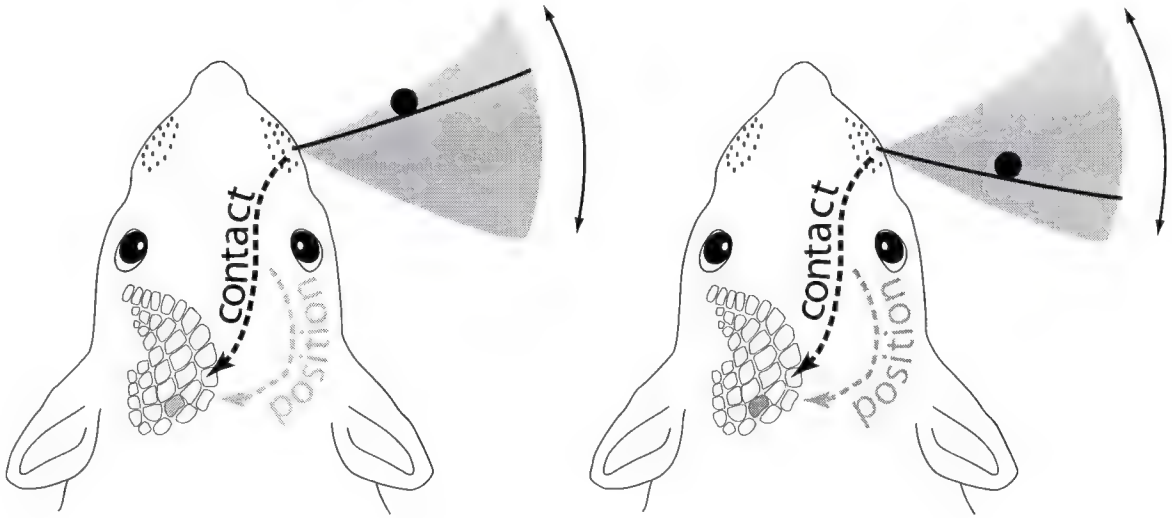


What class of algorithms are used to decode object location?

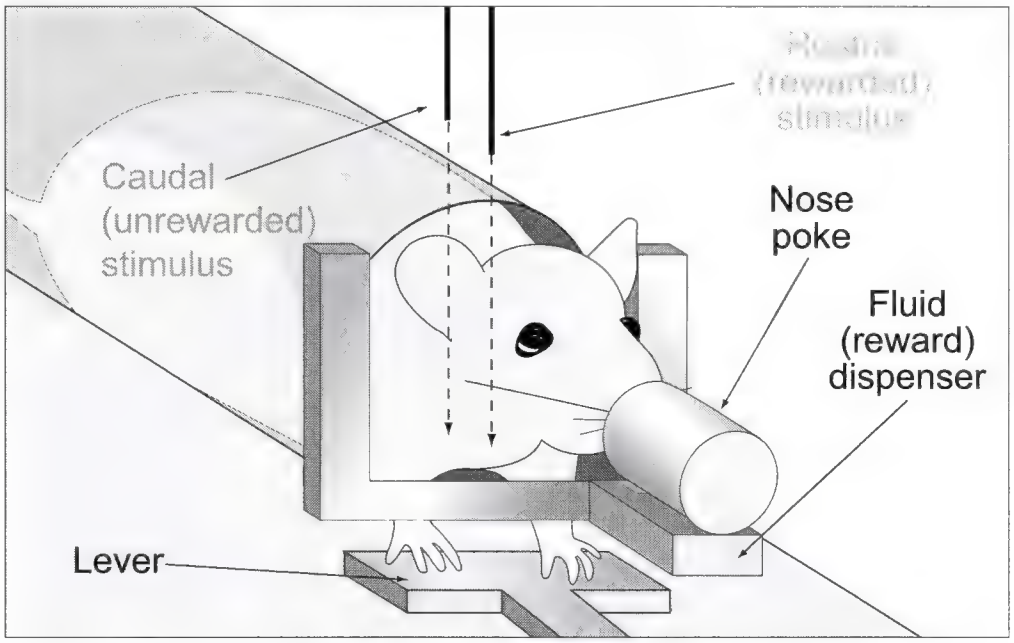
Labeled line and triangulation schemes: Require multiple vibrissae

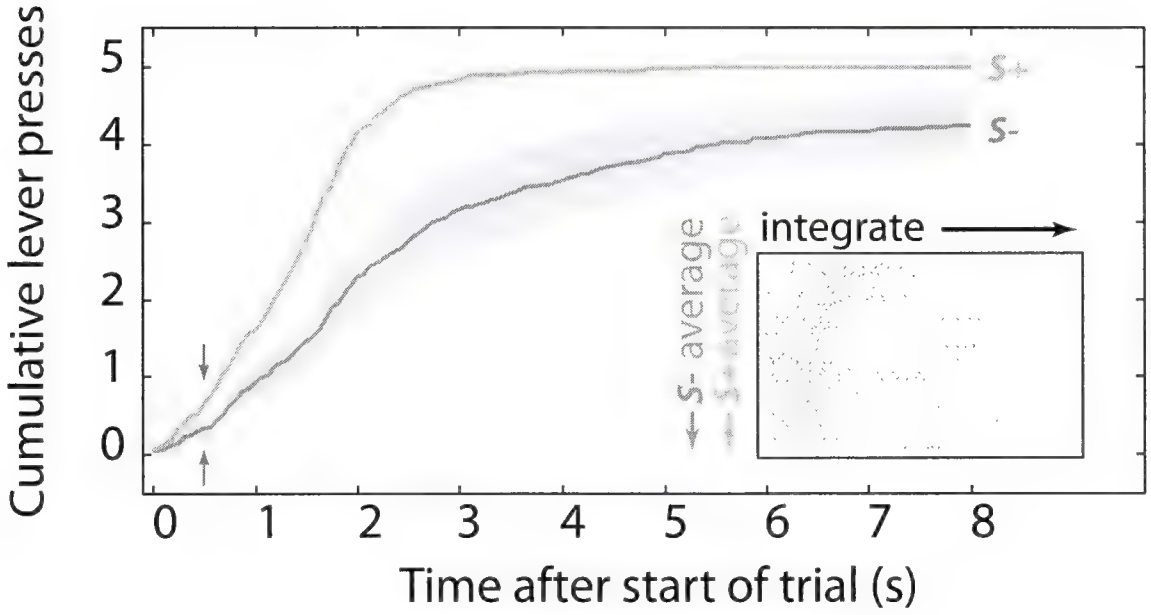


Reafference or efference copy (reference) schemes: Require only a single vibrissa



Rats can distinguish angular position, relative to their face, with a single vibrissa





Mehta, Whitmer, Figueroa, Williams and Kleinfeld (2007)

Lesson 1

Rats can detect location in face-centered coordinates

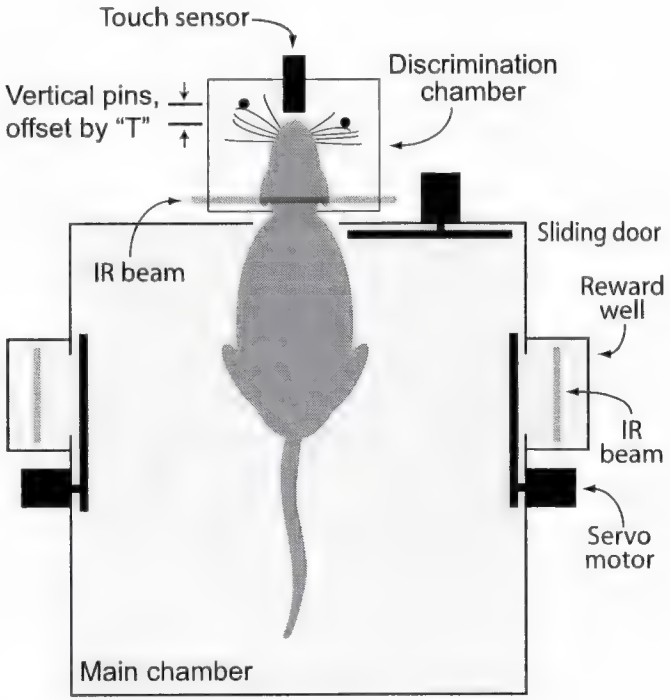
Implies that rats can code the azimuthal position of a vibrissae

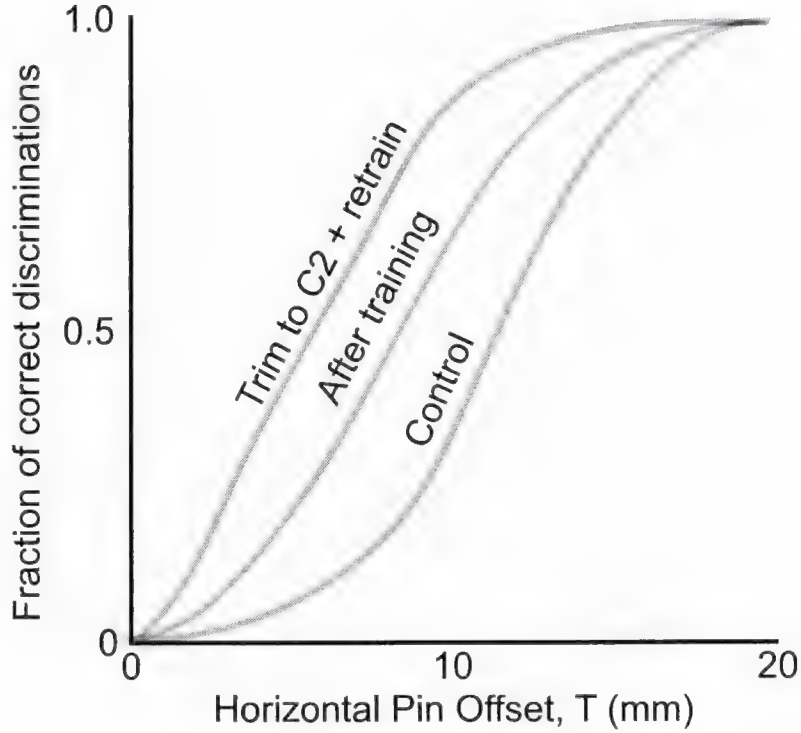
Query

What is the acuity of azimuthal coding?

Accuity of the reference signal is at least 15º (Mehta et al. 2007)

A more stringent estimate of ~ 6º is found with a right/left discrimination task and the assumption that touch on each side is computed with respect to a reference signal (Knutsen, Pietr and Ahissar 2006)

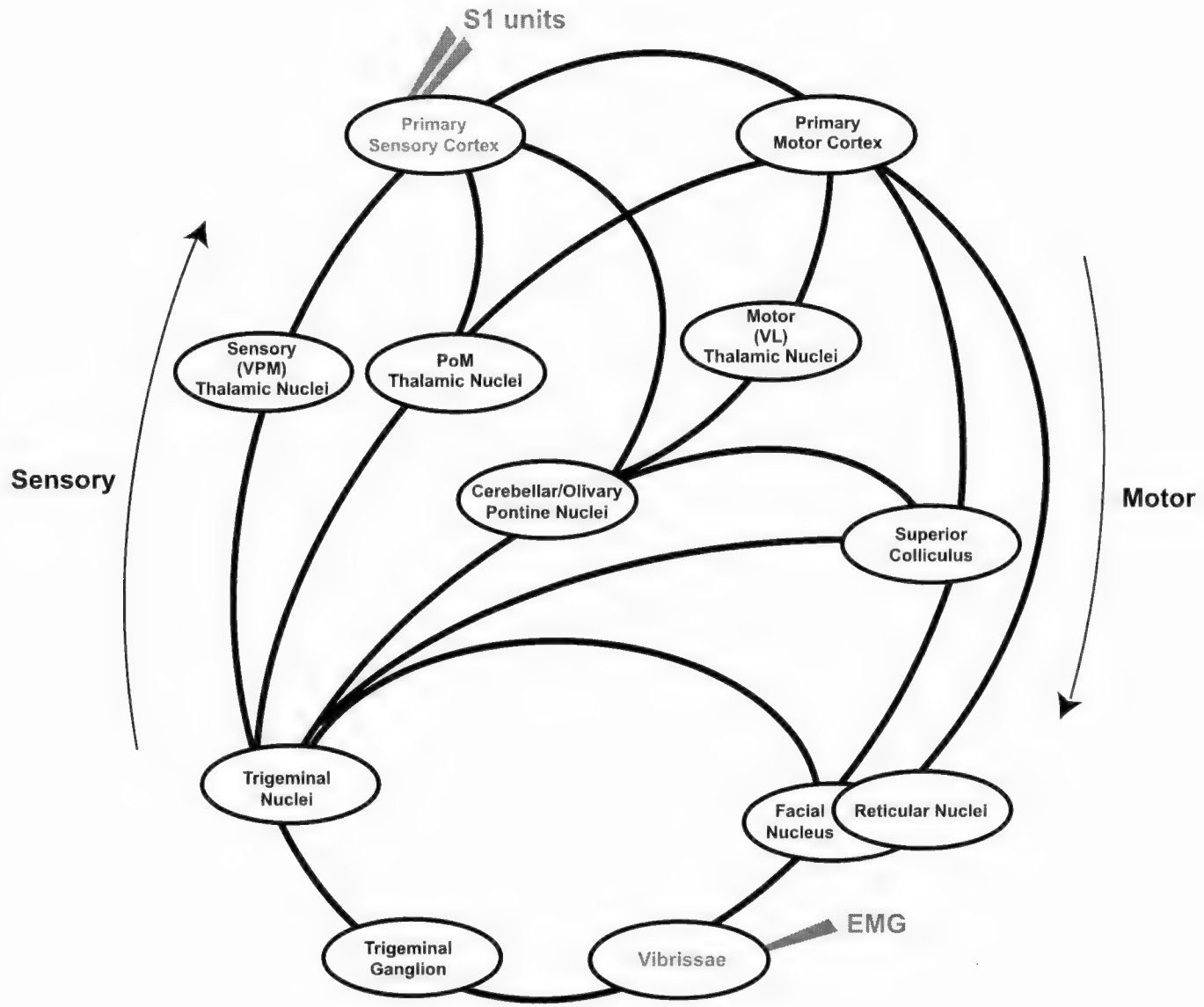




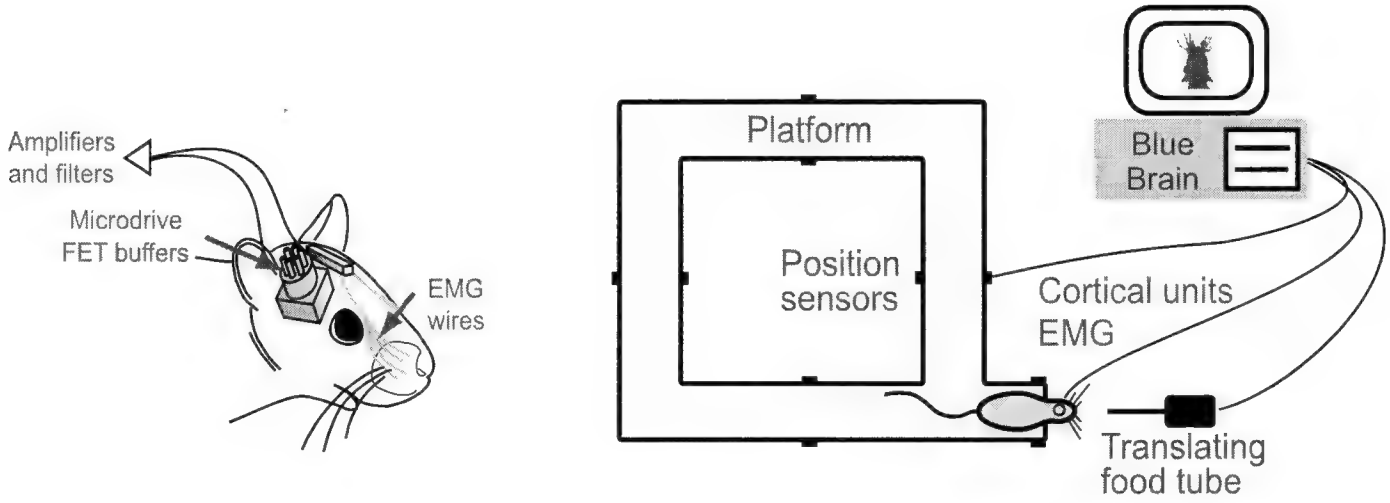
Coding object location in the vibrissa scanning sensorimotor system

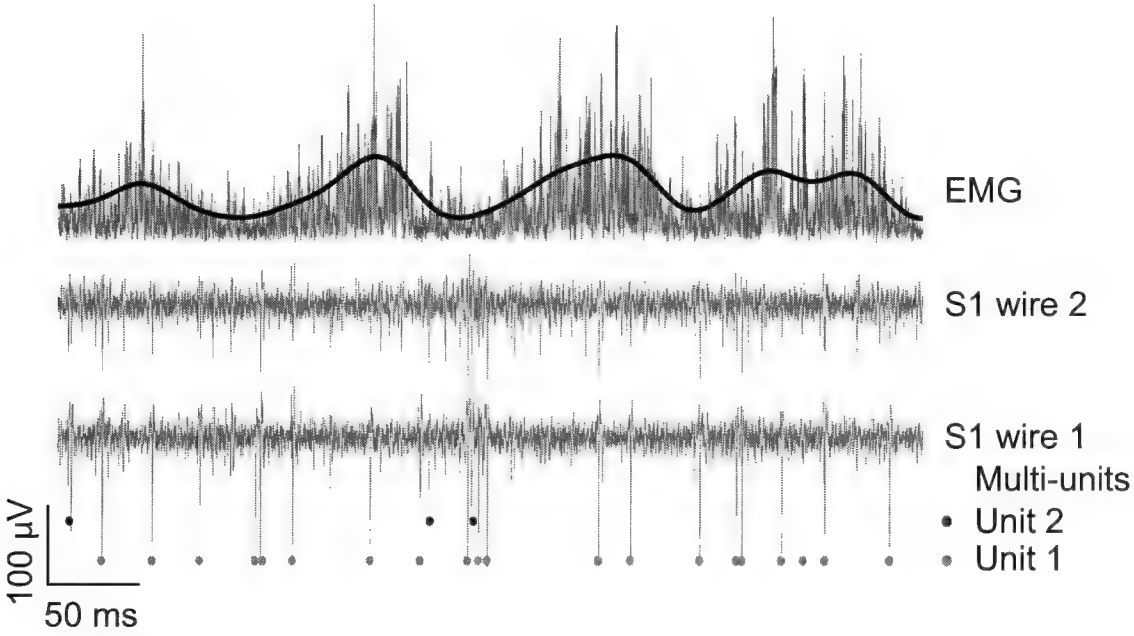
- Psychophysics of localization
- **Neurological basis of position signals**
- Neurological basis of position dependent touch signals
- Coordinate representation in sensory (S1) versus motor (M1) areas

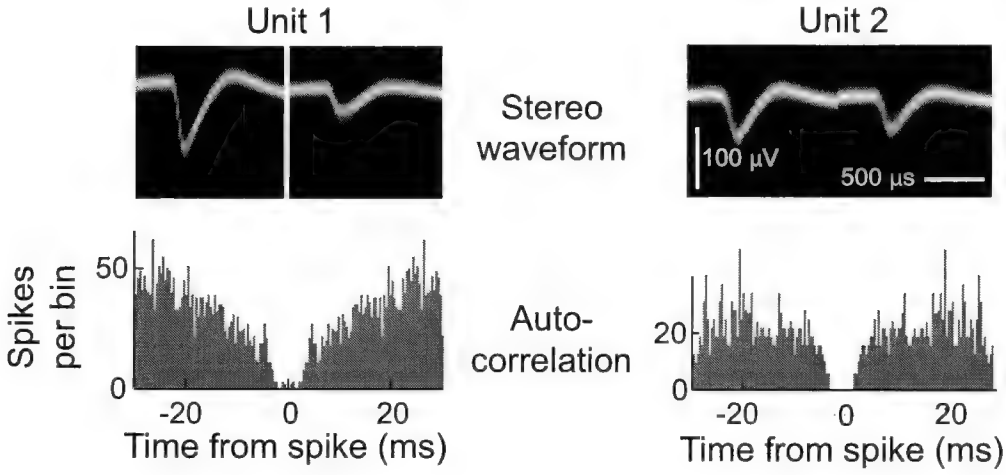
Relation of spiking in S1 cortex to EMG activity during rhythmic whisking in air



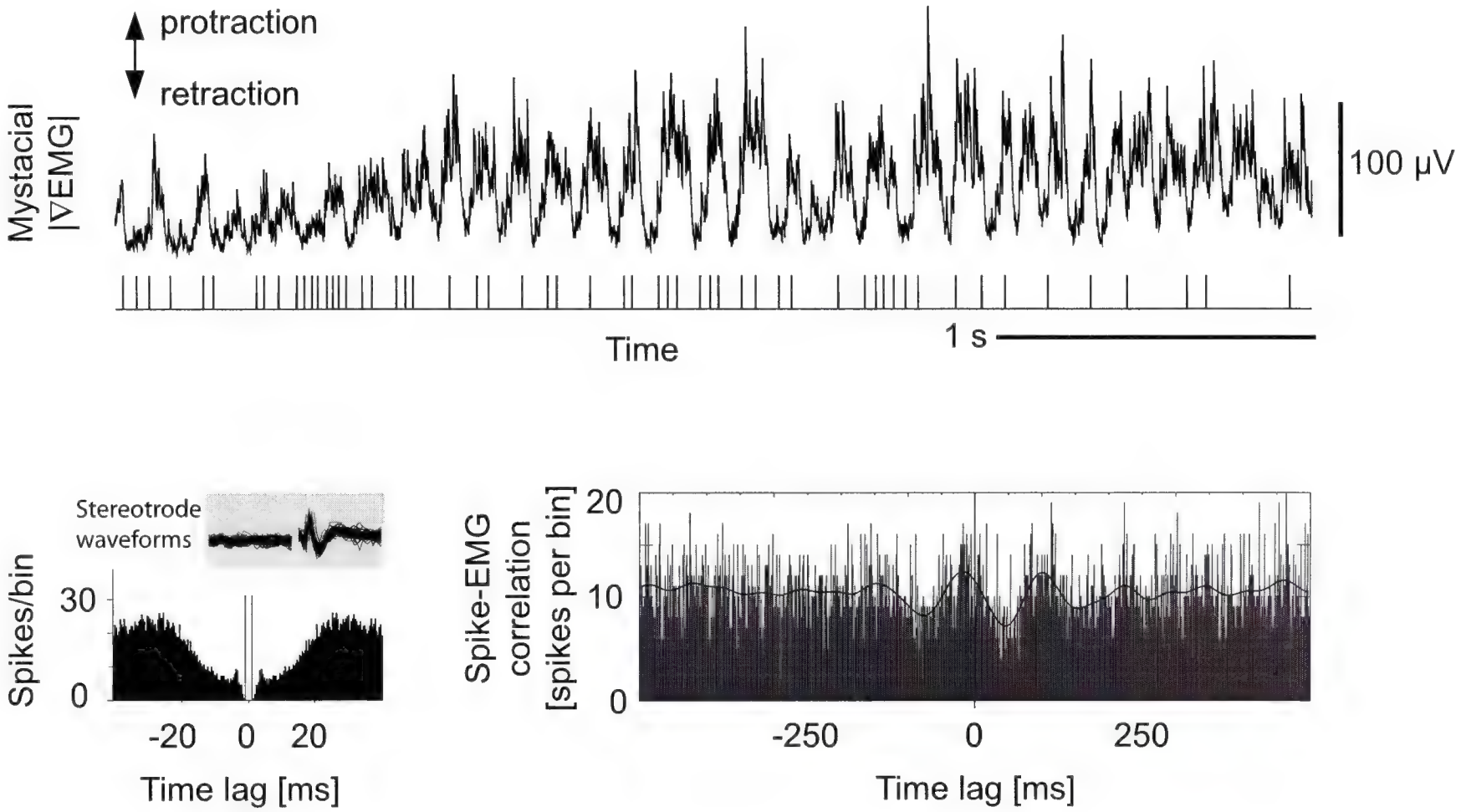
Simultaneous recording of vibrissa EMG and single units in S1 vibrissa cortex



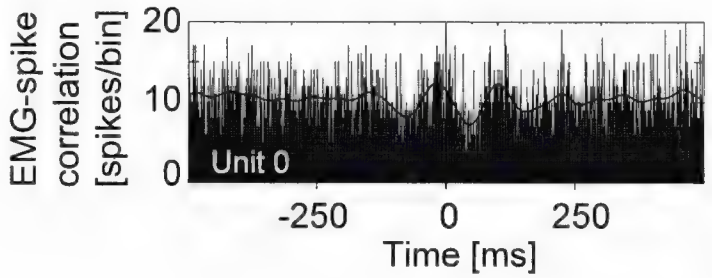


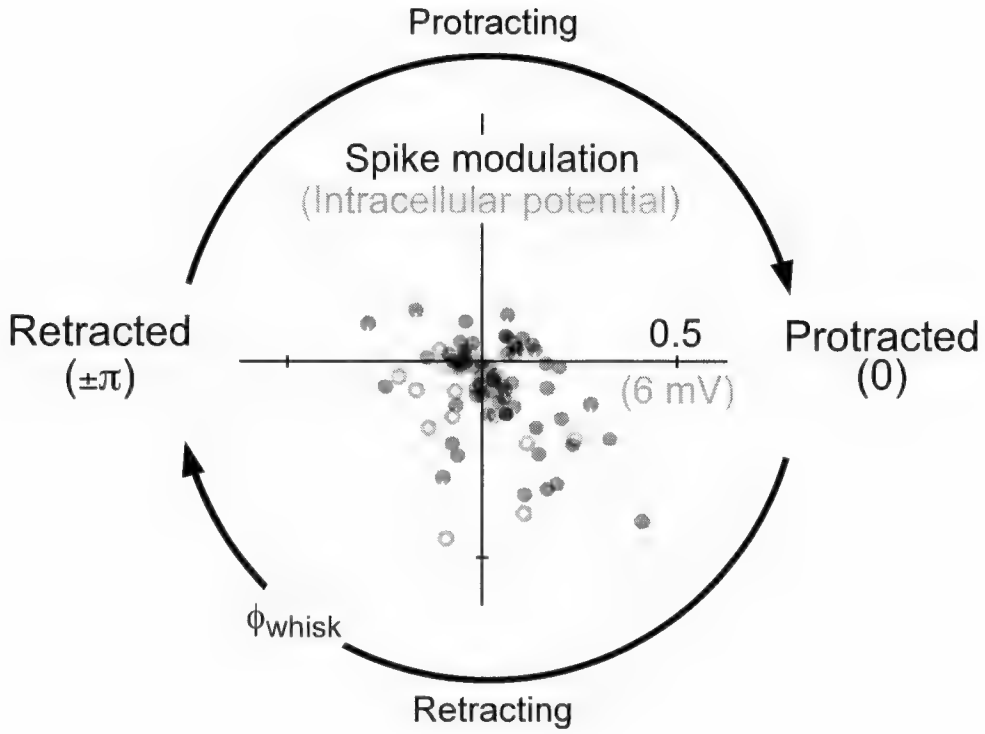


Simultaneous records of EMG and single units in S1 cortex as rats whisk in air reveal a reference signal of vibrissa position



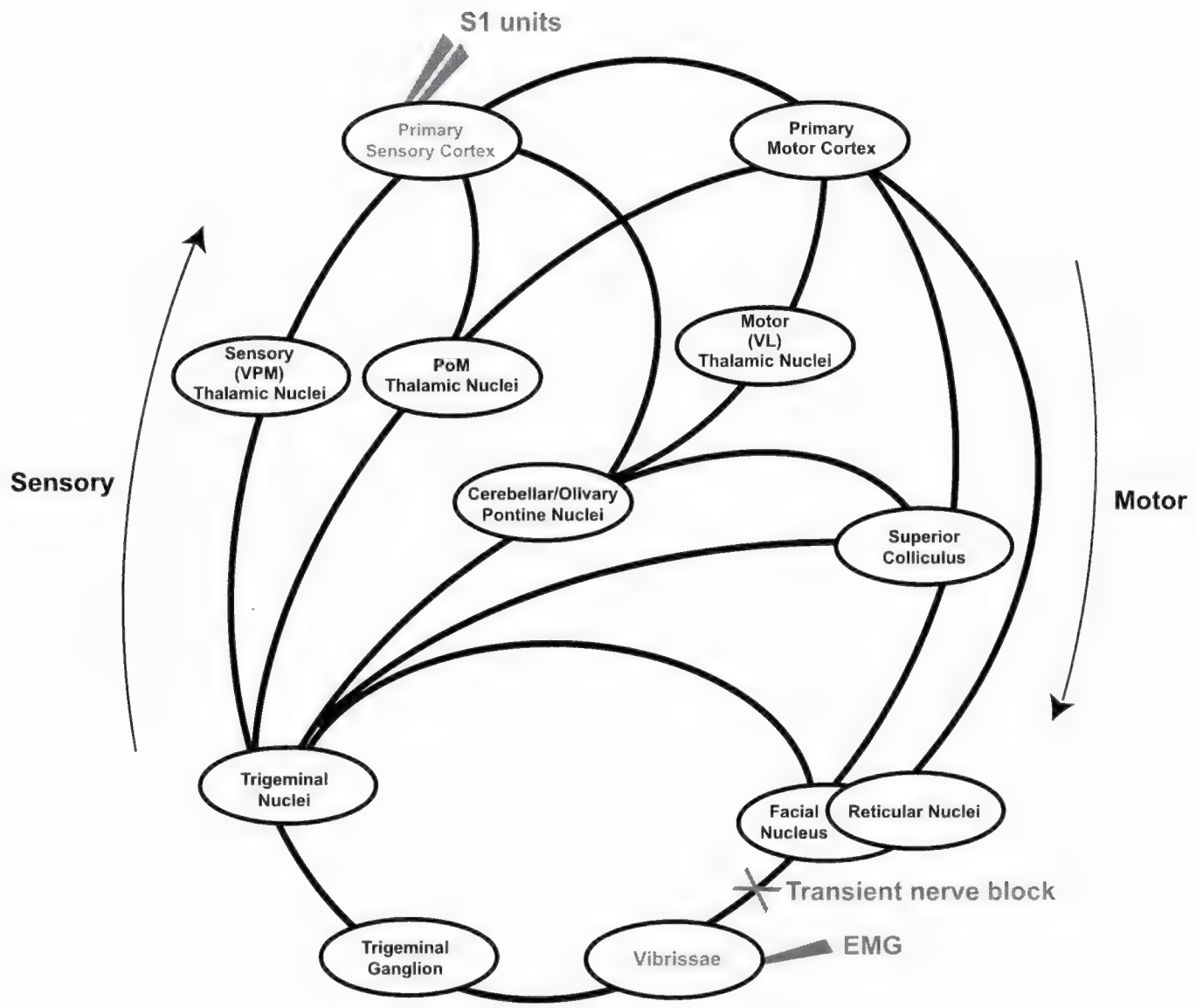
Individual neurons encode a specific phase in the whisk cycle
All phases are coded



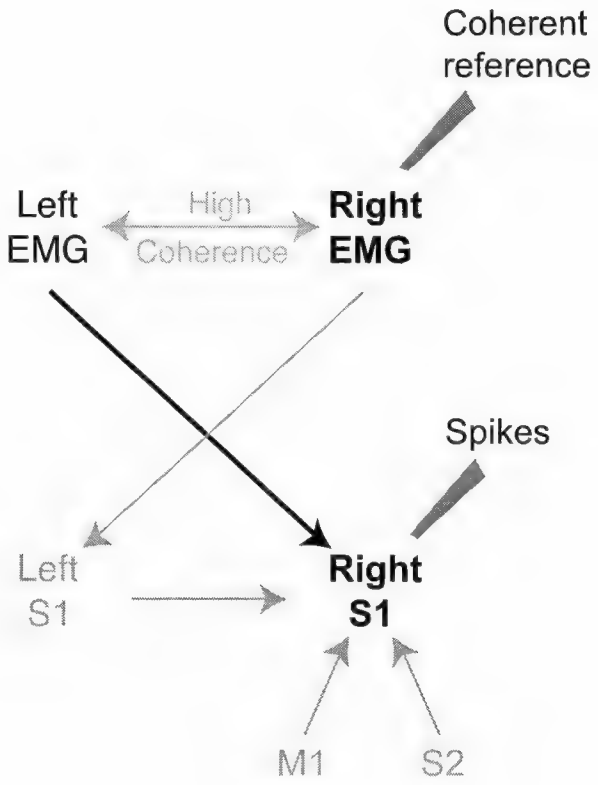


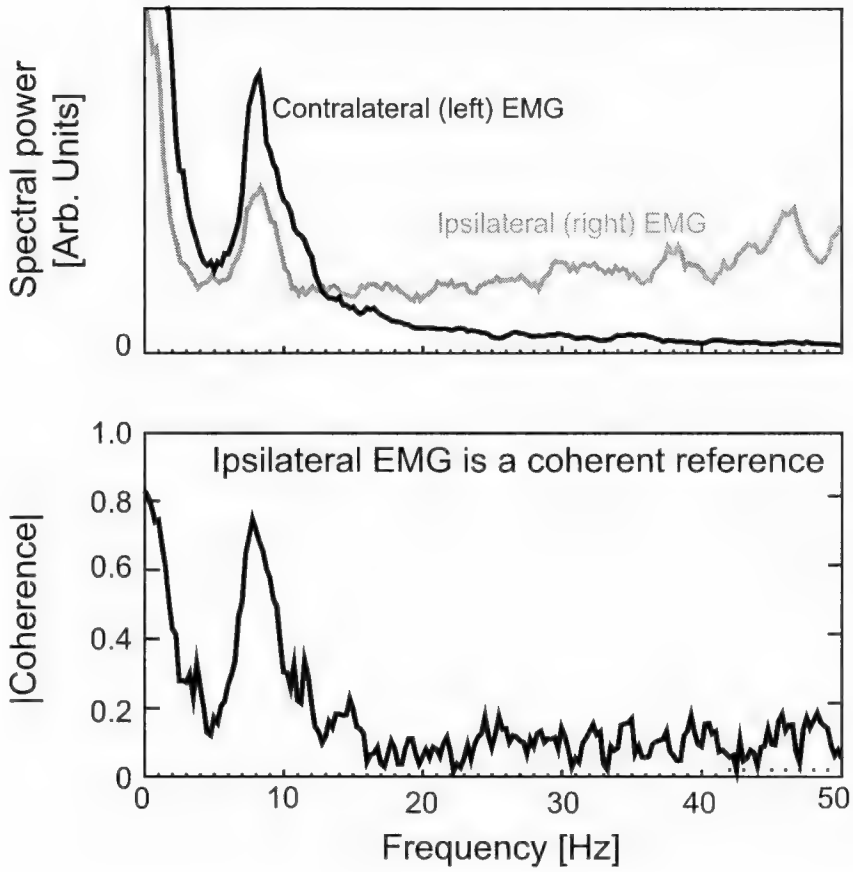
Fee, Mitra & Kleinfeld 1997; O'Connor, Berg & Kleinfeld 2001; Ganguly & Kleinfeld 2004; Crochet & Petersen 2006; Curtis & Kleinfeld 2009

Does the reference originate from peripheral reafference *or* efference copy?



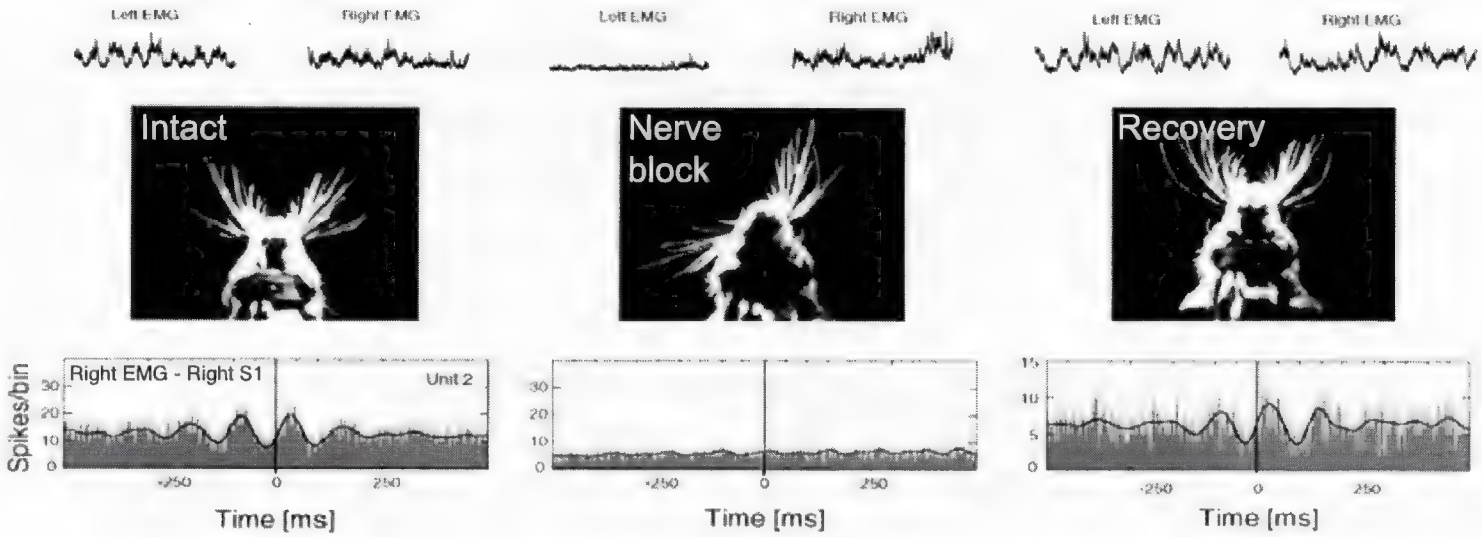
Facial nerve block to determine if the reference signal in S1 cortex originates from peripheral reafference *or* efference copy





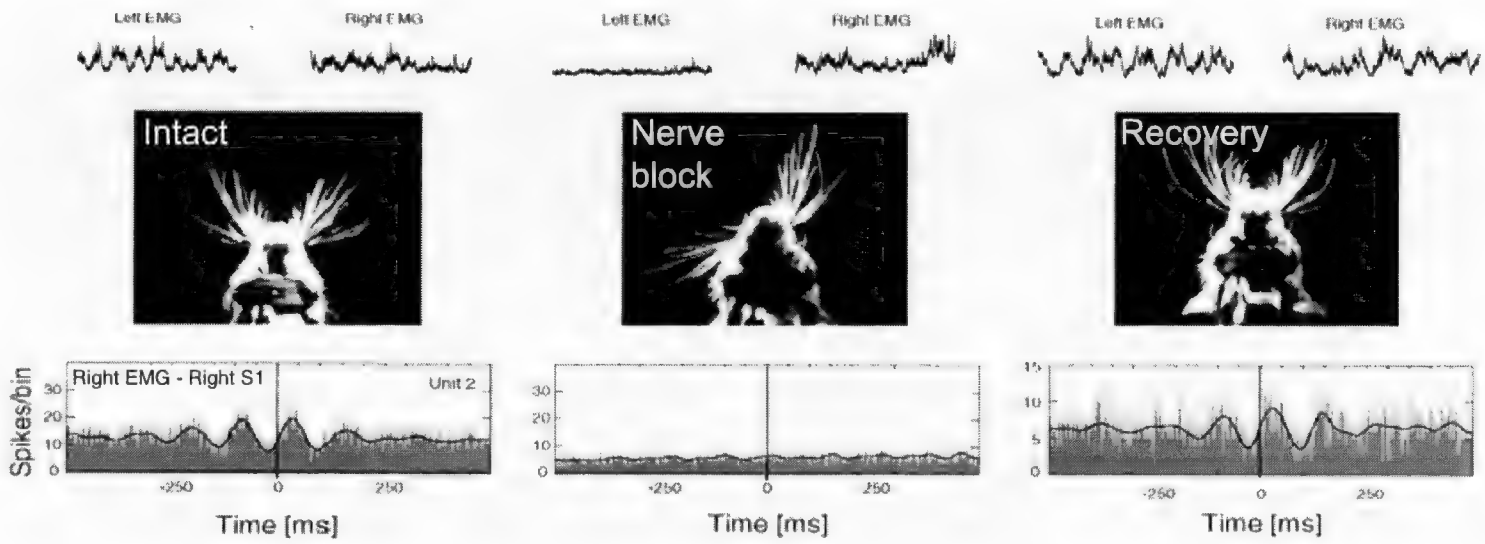
Fee, Mitra and Kleinfeld (1997)

Coherence between vibrissa phase and spiking in S1 cortex originates from peripheral reafference (*not* efference copy)

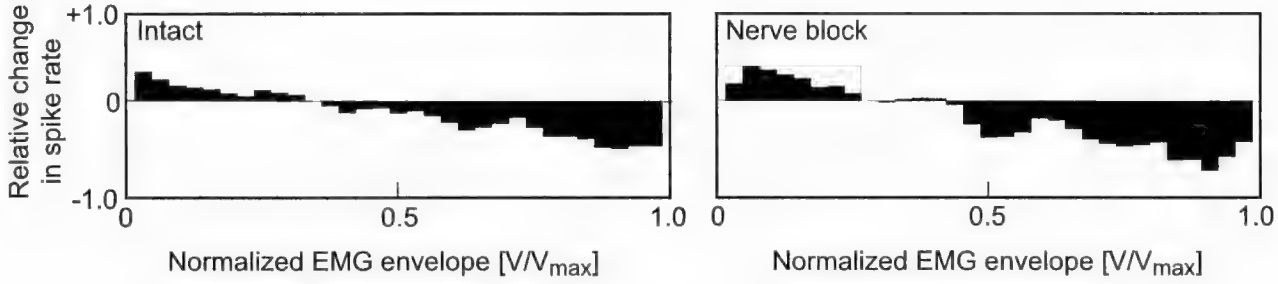


Fee, Mitra and Kleinfeld (1997)

Coherence between vibrissa phase and spiking in S1 cortex originates from peripheral reafference (*not* efference copy)



In contrast, coherence between the envelope of vibrissa position and spiking in S1 cortex depends on efference copy



Fee, Mitra and Kleinfeld (1997)

Lesson 2

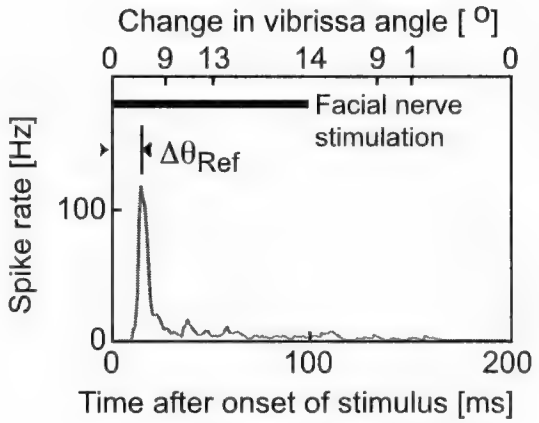
S1 neurons code azimuth – each neuron with preferred "phase"

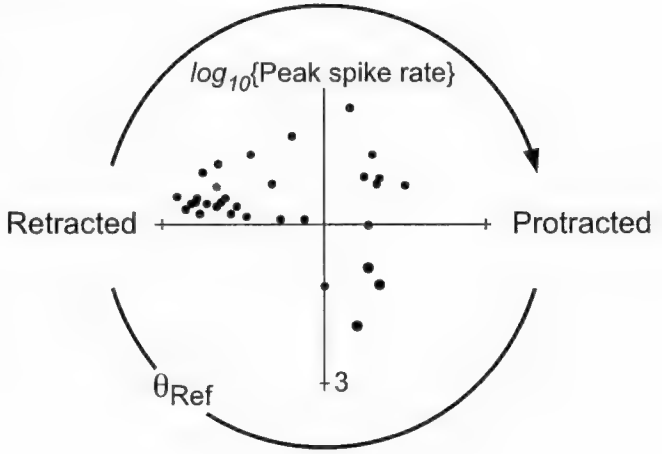
Coding is by peripheral reafference

Query

Is there a separate "phase" versus "touch" sensory pathway?

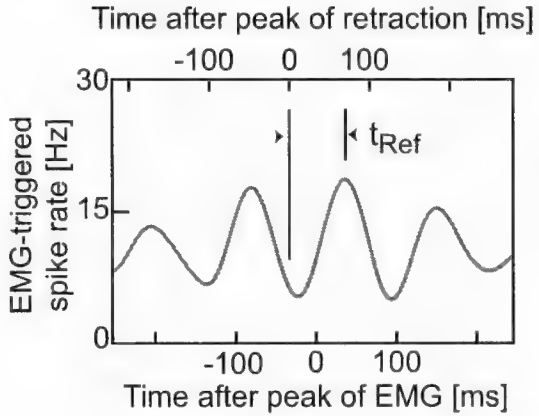
Neurons in the trigeminal ganglion first code angular coordinates (Szwed, Bagdasarian & Ahissar 2003)

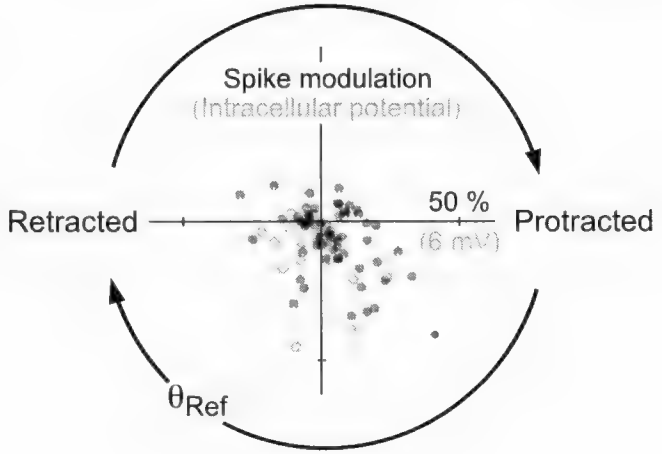




Compare with neuronal response in S1 cortex

(Extracellular: Fee, Mitra & Kleinfeld 1997; Intracellular: Crochet & Petersen 2006)



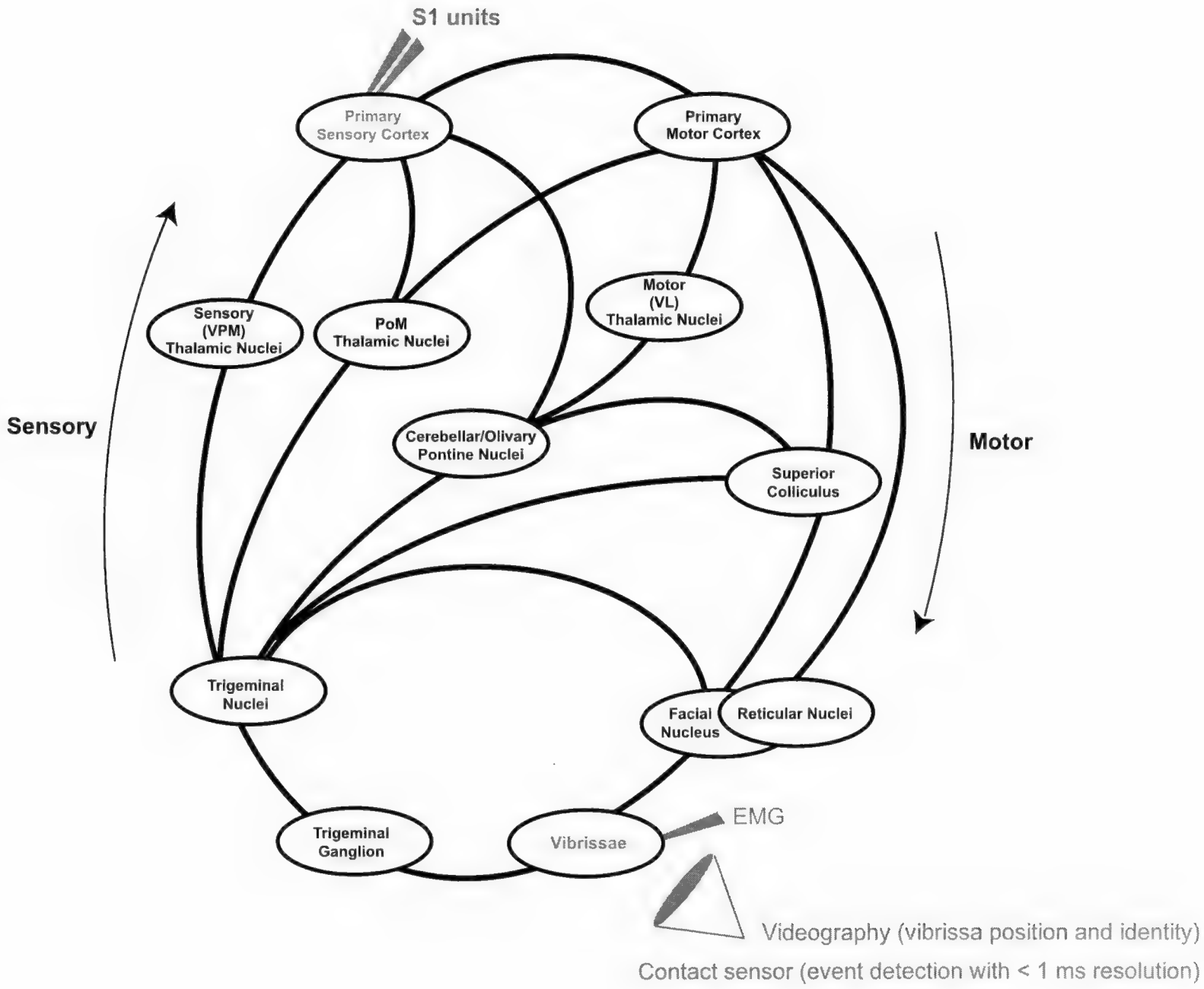


Mehta and Kleinfeld (Neuron 2004); Kleinfeld, Ahissar and Diamond (Current Opinion in Neurobiology 2006)

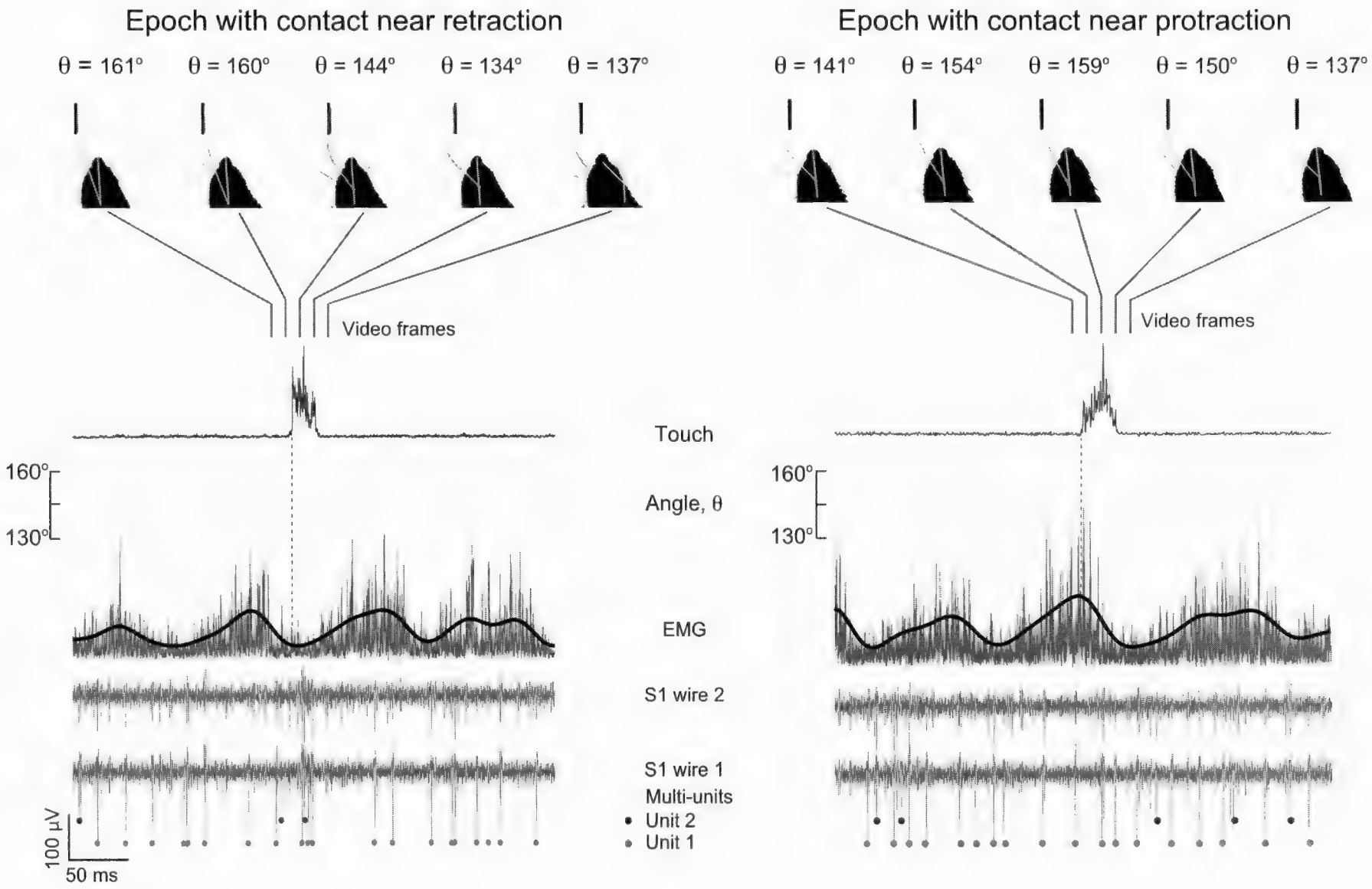
Coding object location in the vibrissa scanning sensorimotor system

- Psychophysics of localization
- Neurological basis of position signals
- **Neurological basis of position dependent touch signals**
- Coordinate representation in sensory (S1) versus motor (M1) areas

Relation of touch response in S1 to phase and position in the whisk cycle

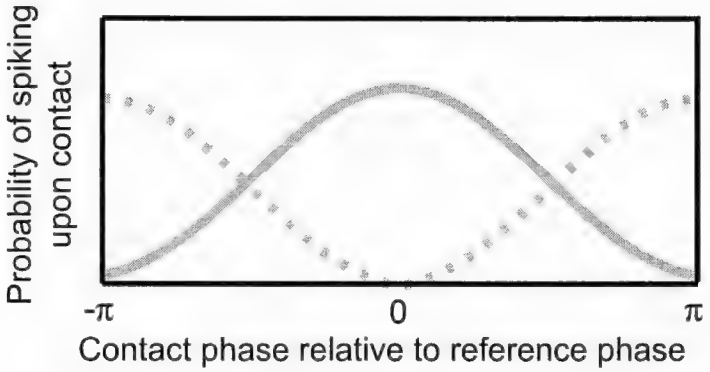


Simultaneous recording of vibrissa EMG, position, and touch, along with single unit activity in S1 cortex



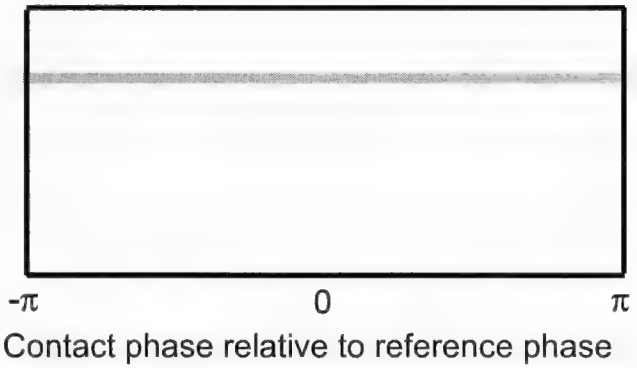
Is vibrissa touch response conditioned on phase in the whisk cycle?

Interacting phase & touch signals



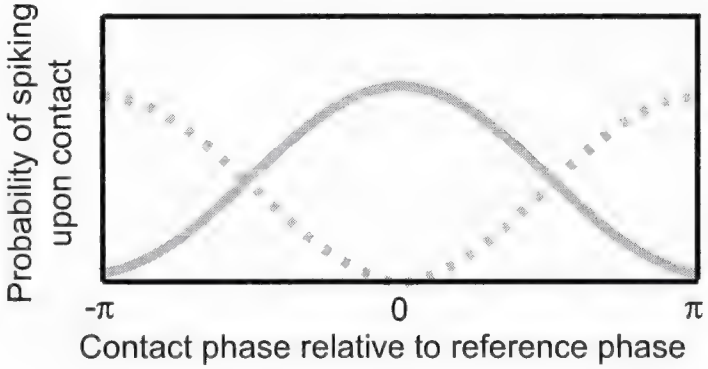
versus

Non-interacting phase & touch signals



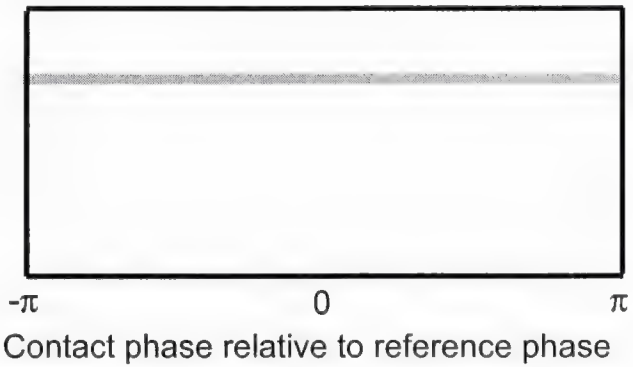
Is vibrissa touch response conditioned on phase in the whisk cycle?

Interacting phase & touch signals

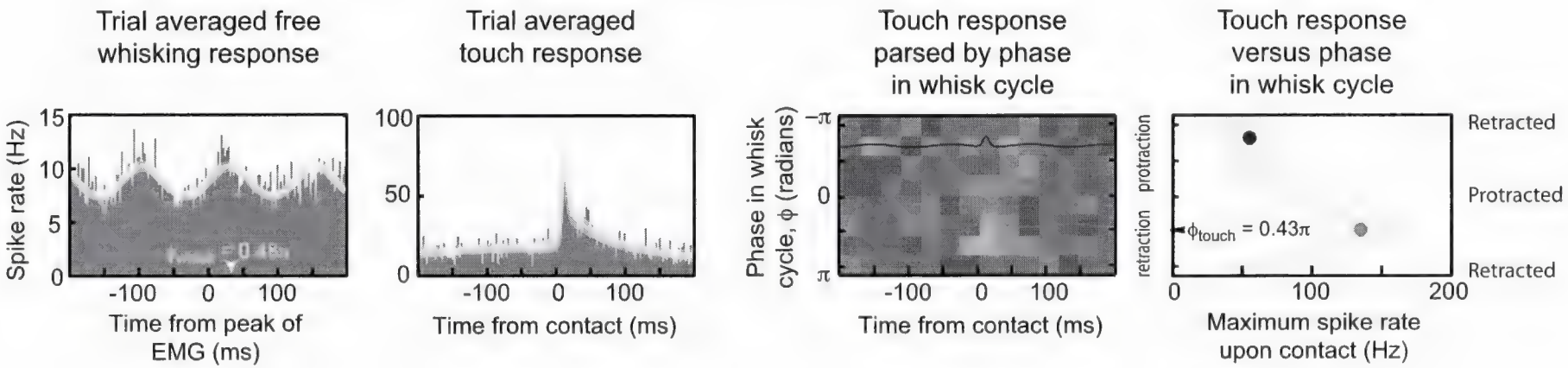


versus

Non-interacting phase & touch signals

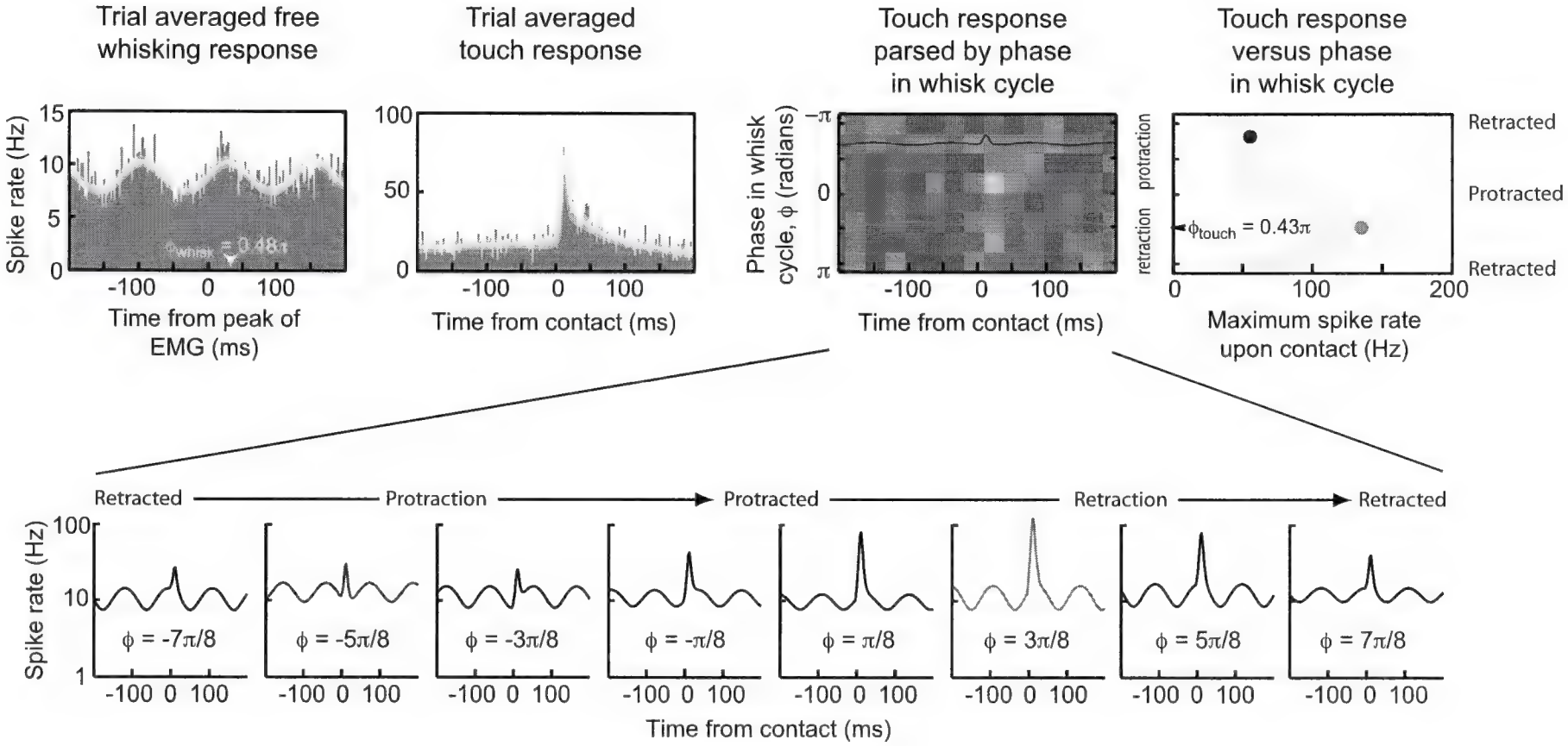


Yes! - Interacting phase & touch signals with $\phi_{touch} = \phi_{whisk}$



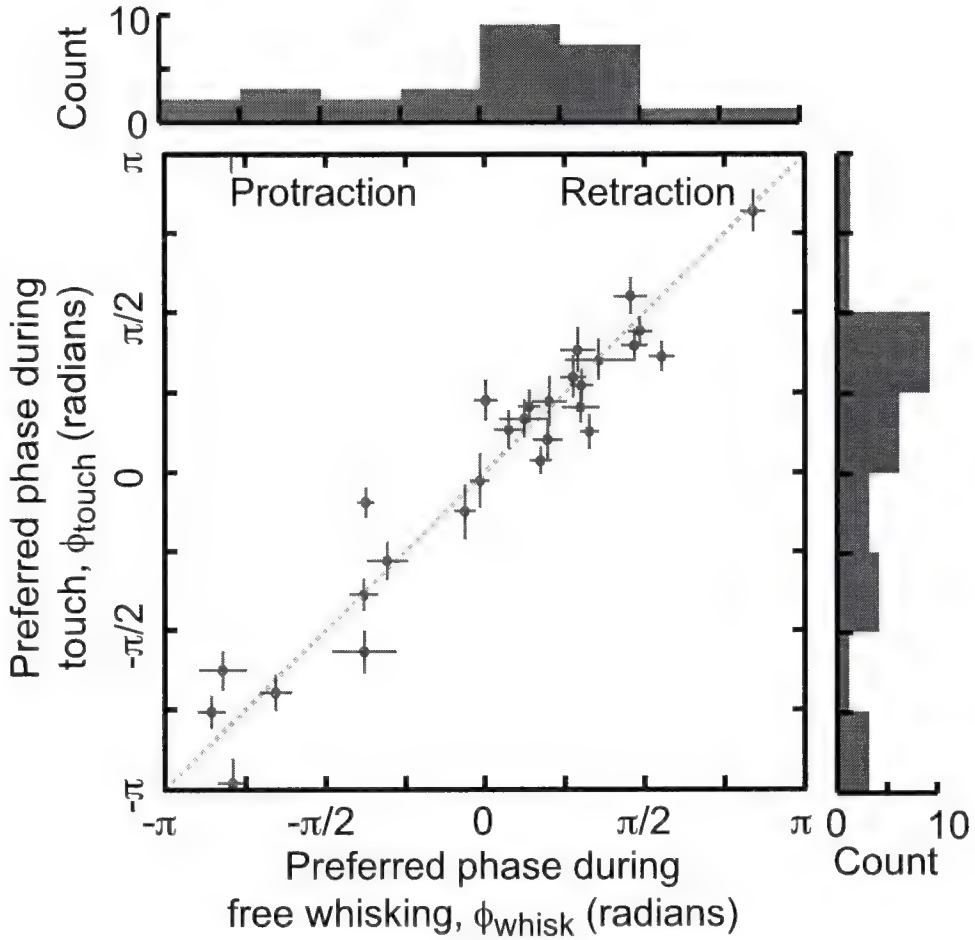
Curtis and Kleinfeld (2009)

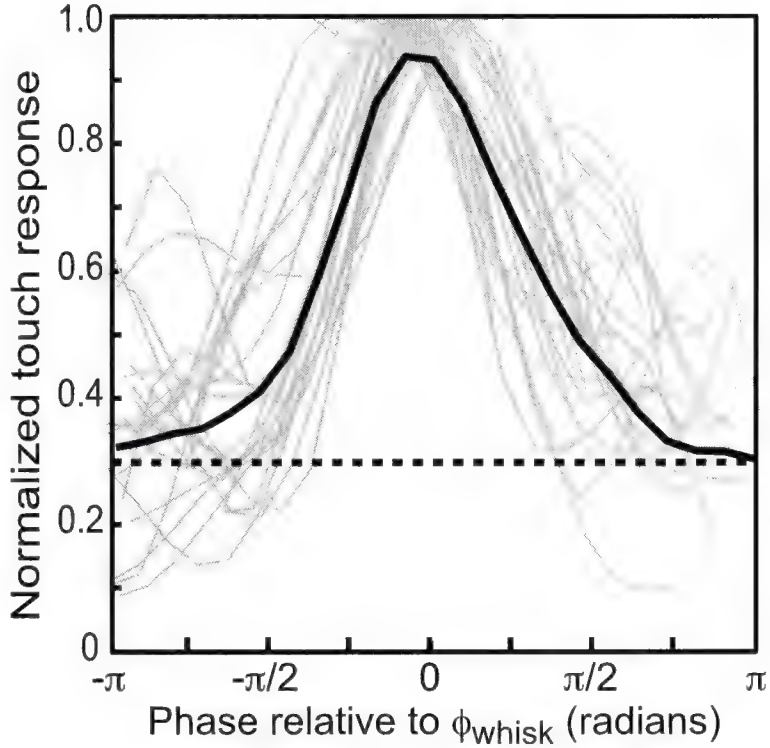
Vibrissa touch response is conditioned on phase in the whisk cycle



Curtis and Kleinfeld (2009)

Touch signals in S1 cortex are conditioned on phase in the whisk cycle during active touch with trained rats

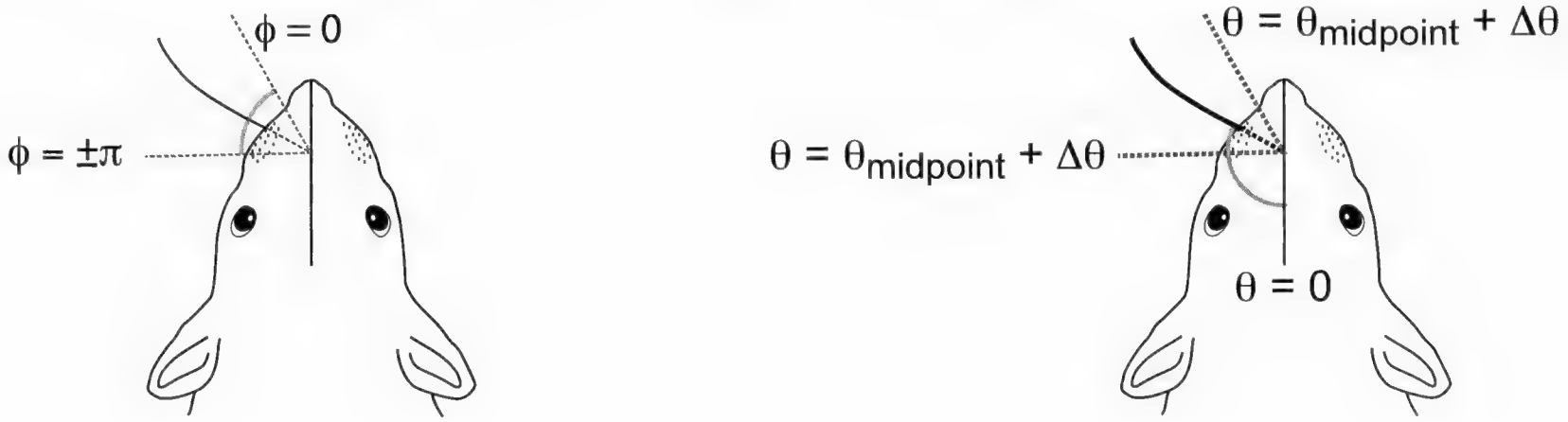




Curtis and Kleinfeld (2009)

Is the vibrissa touch response conditioned solely by phase?

Touch referenced to phase vs. **Touch referenced to position**



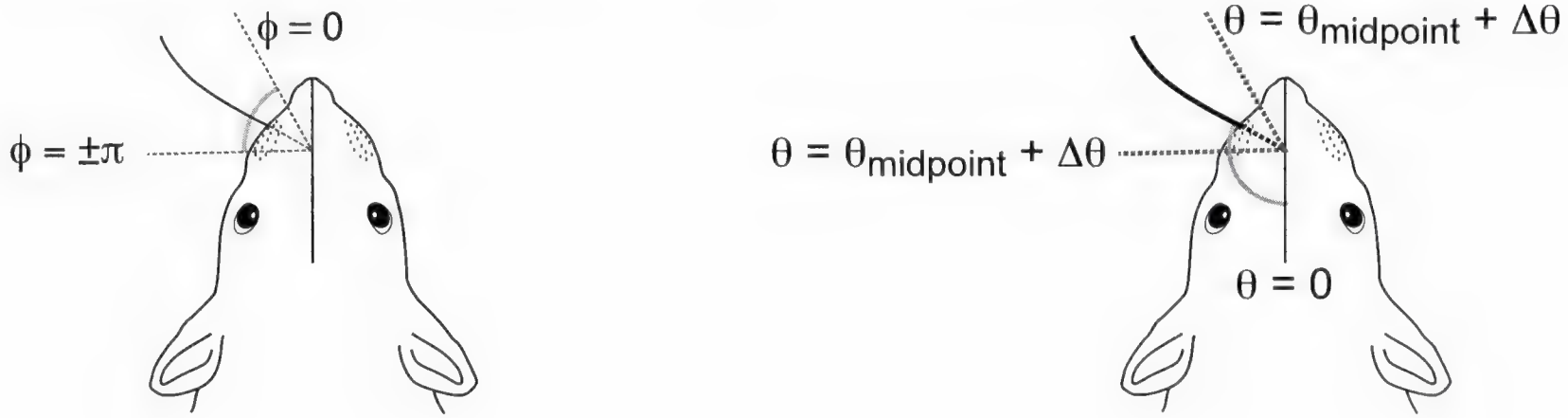
$$\theta(t) = \theta_{midpoint} + \Delta\theta \cos \phi(t)$$

where

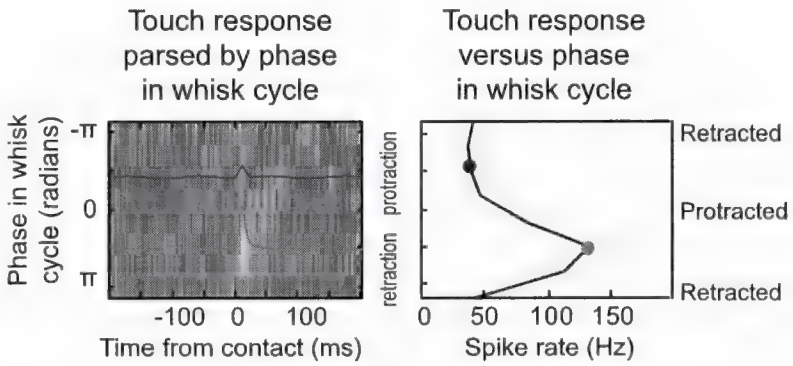
$$\phi(t) = 2\pi f_{whisk}\, t + \phi_{whisk}$$

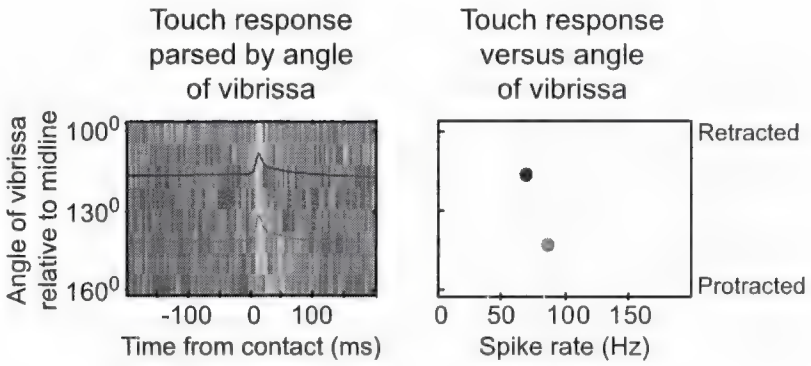
Is the vibrissa touch response conditioned solely by phase?

Touch referenced to phase **vs.** **Touch referenced to position**



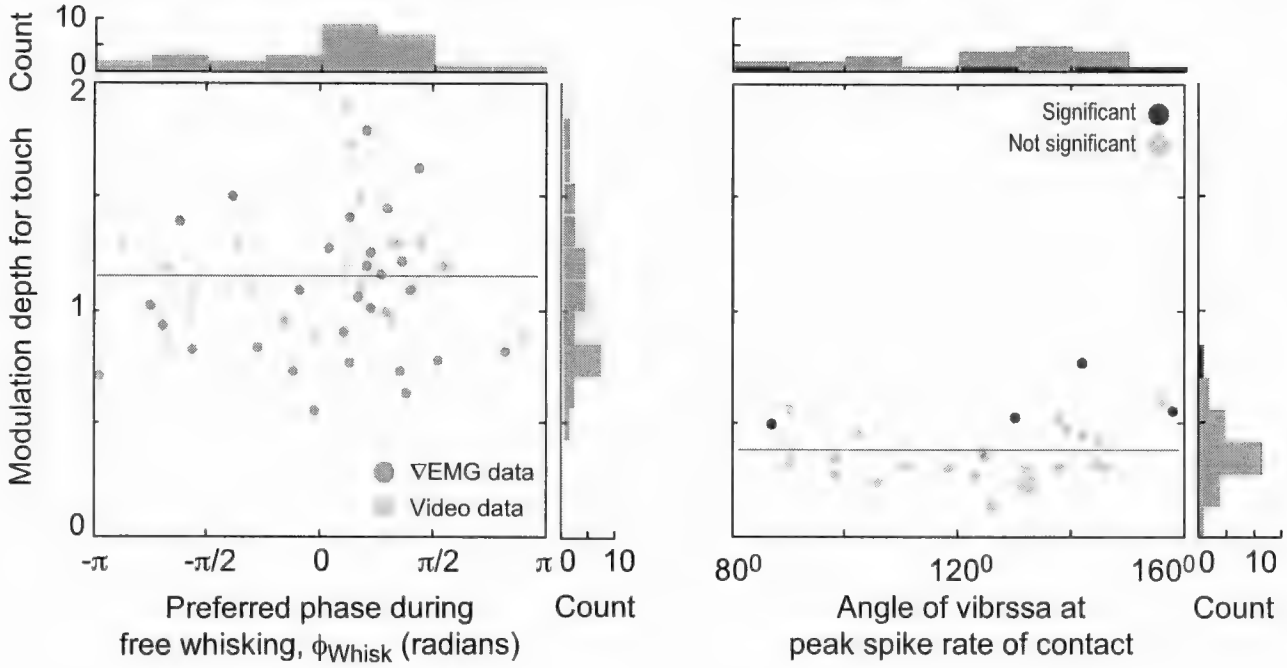
Yes! - tuning depends on phase, ϕ, and not angular position, θ

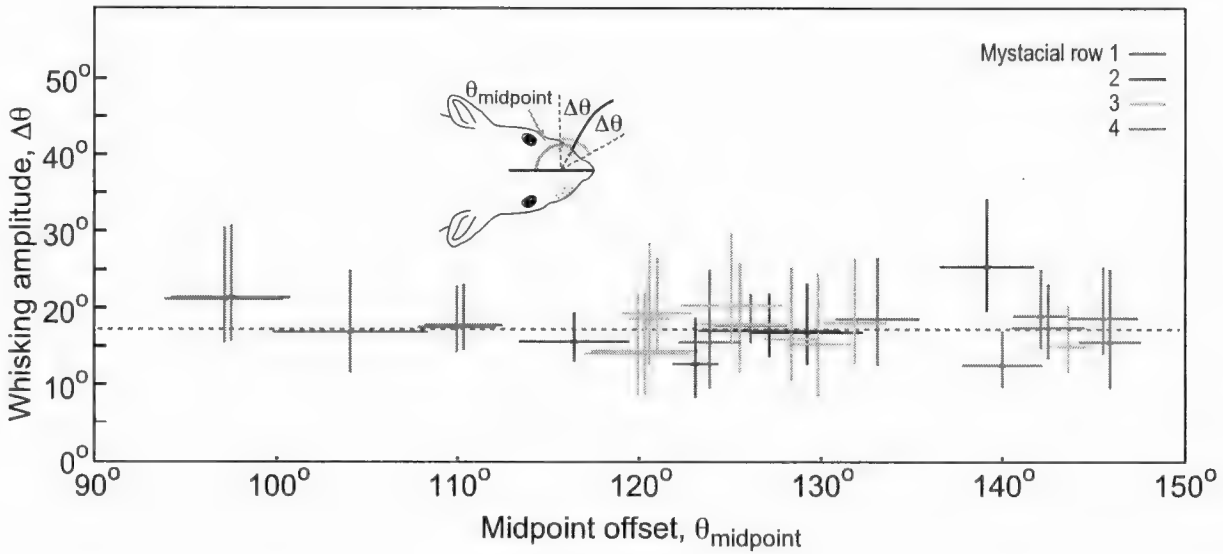




Curtis and Kleinfeld (2009)

Vibrissa touch response is conditioned on phase and *not* position





Curtis and Kleinfeld (2009)

Lesson 3

Touch is coded by contact conditioned on vibrissa coordinate

S1 cortex codes touch in “phase” versus “angle” coordinates

Query

What is the potential advantage of “phase” over “angle”?

Efficiency versus ambiguity in phase coding (`a la Fairhall et al. 2001)

Coding in absolute angle

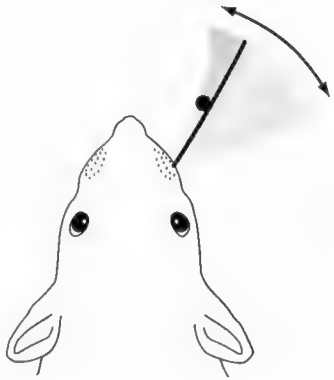
$\theta(t) = \theta_{midpoint} + \Delta\theta \cos \phi(t)$

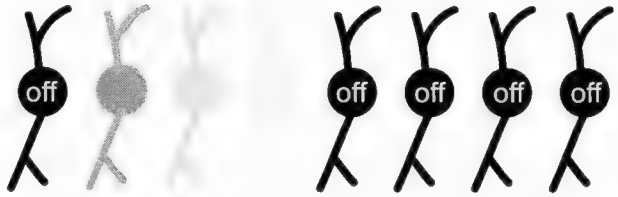
Inefficient but unambiguous

Coding normalized by phase

$\phi(t) = [2\pi f_{whisk} t + \phi_{touch}]$ *modulo* 2π

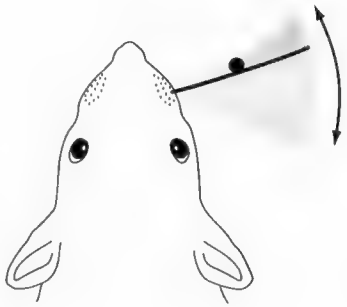
Efficient but ambiguous





Color labels angle

Color labels phase

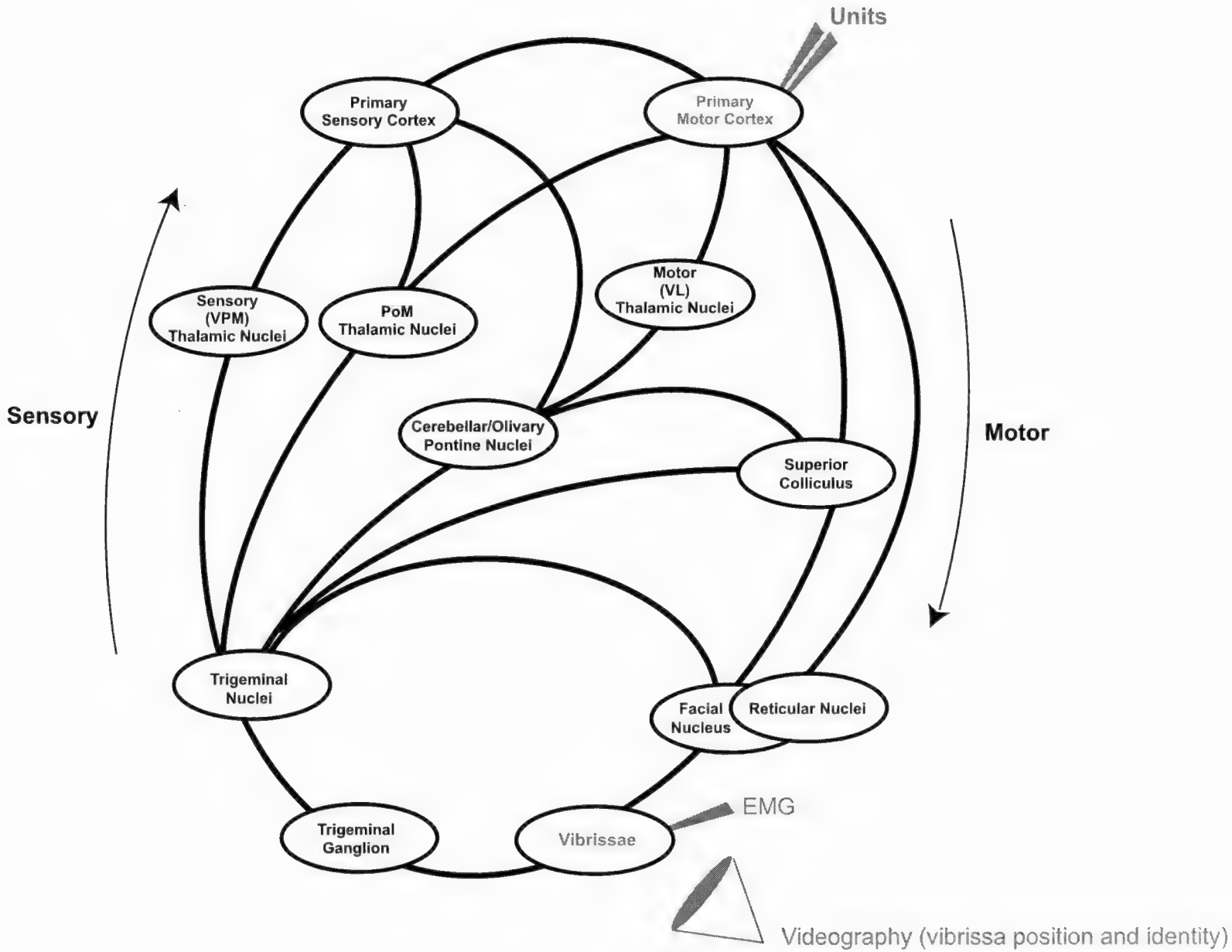


What is the mechanism for phase representation? Where are $\theta_{midpoint}$ and $\Delta\theta$ represented?

Coding object location in the vibrissa scanning sensorimotor system

- Psychophysics of localization
- Neurological basis of position signals
- Neurological basis of position dependent touch signals
- **Coordinate representation in sensory (S1) versus motor (M1) areas**

Relation of whisking response in M1 to phase and position in the whisk cycle



Four slides with unpublished data were pulled from the online version

Lesson 4

Motor cortex codes position and offset variables as well as phase

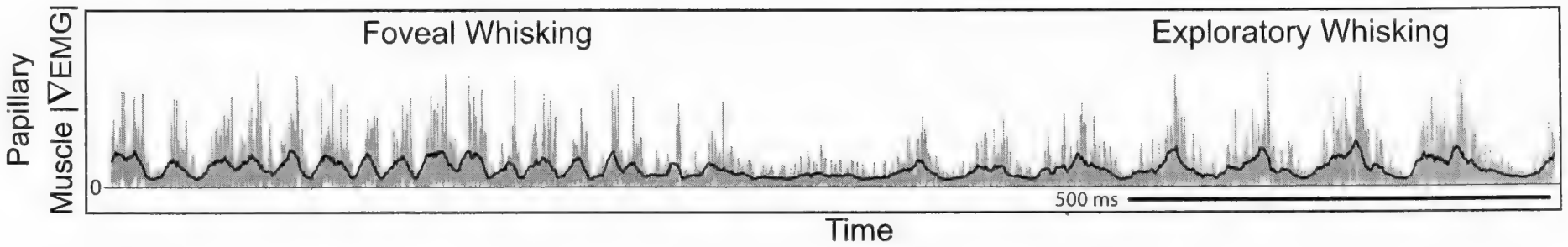
Preliminary data: These slow variables are generated in motor areas

Query

Is face-centered object position computed in M1 cortex?

Modes of whisking by rat

Exploratory whisking, also referred to as symmetric whisking



Asymmetric whisking as a result of contact between the vibrissae and a wall

Berg and Kleinfeld (2003)
Towal and Hartmann (2006)
Mitchinson, Martin, Grant and Prescott (2007)

Summary

Primary sensory cortex computes contact conditioned on phase

Primary motor cortex generates slow whisking parameters

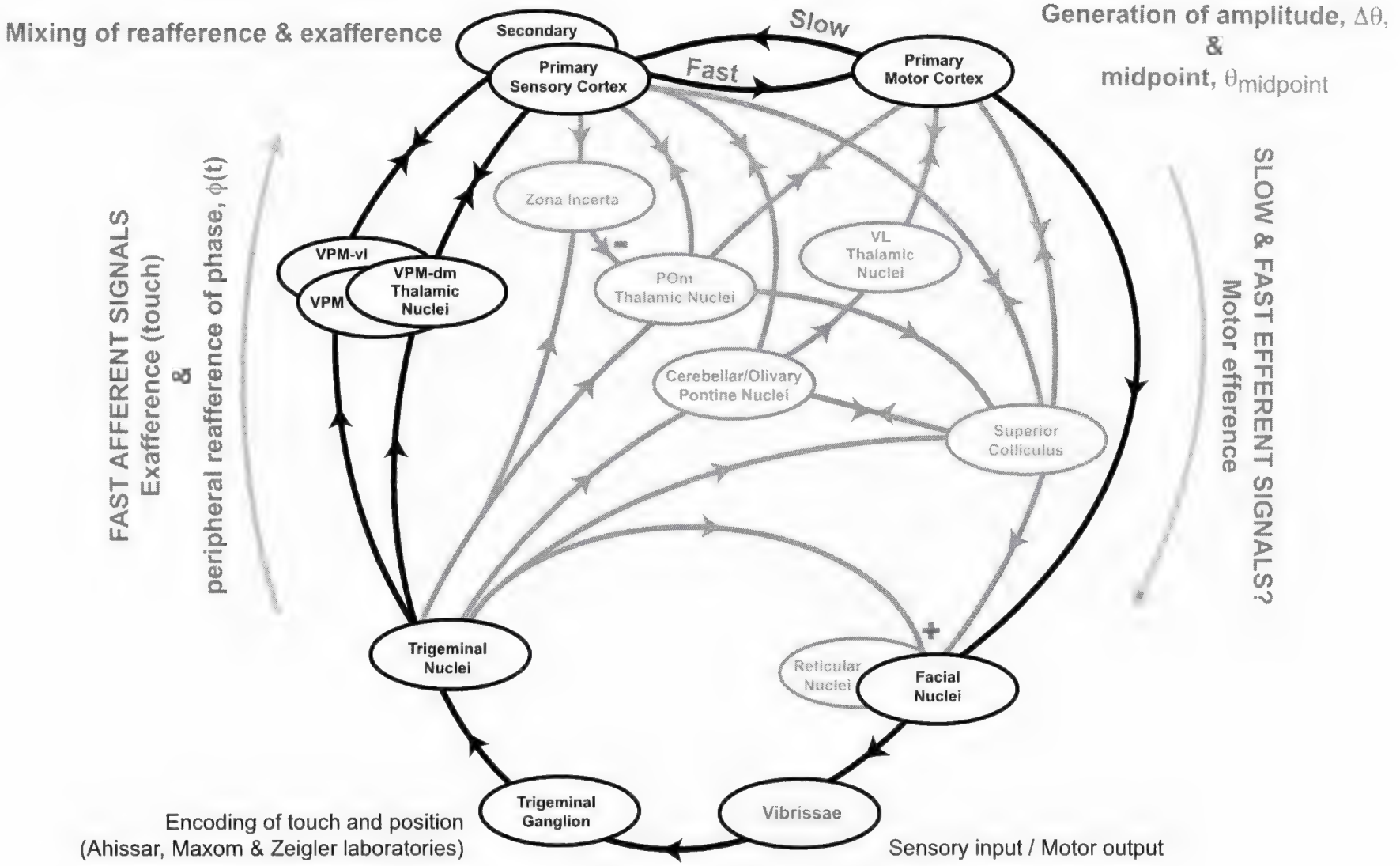
Regions share information

Big questions

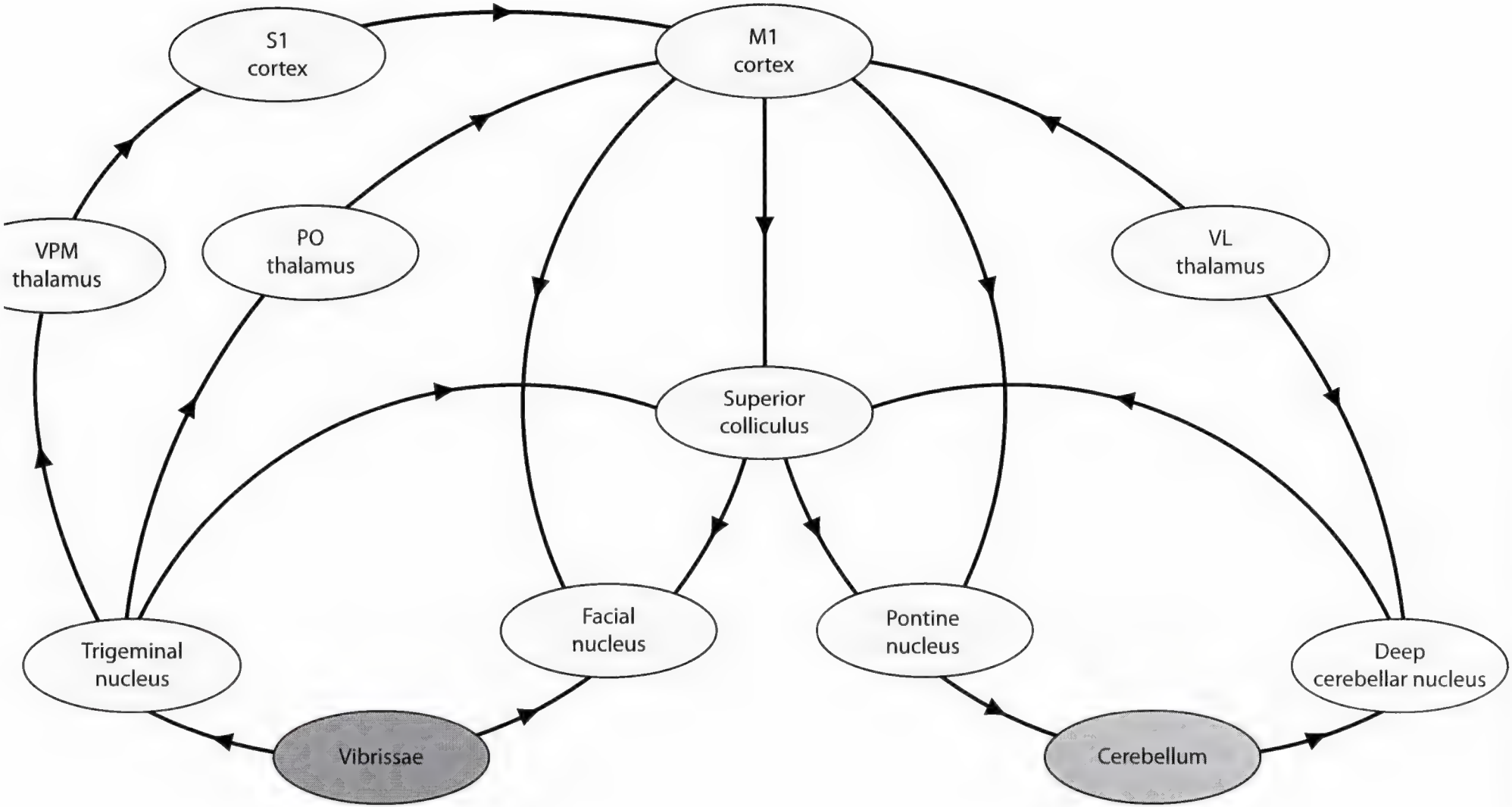
What is the feature set for vibrissa somatosensation?
(What does the rat see with her vibrissae?)

How does signaling in S1 (or ?) change the whisking trajectory?

Synopsis of whisking signals in vibrissa sensorimotor cortical loop



Ehud Ahissar and Peter Redgrave's Conjecture (2009)



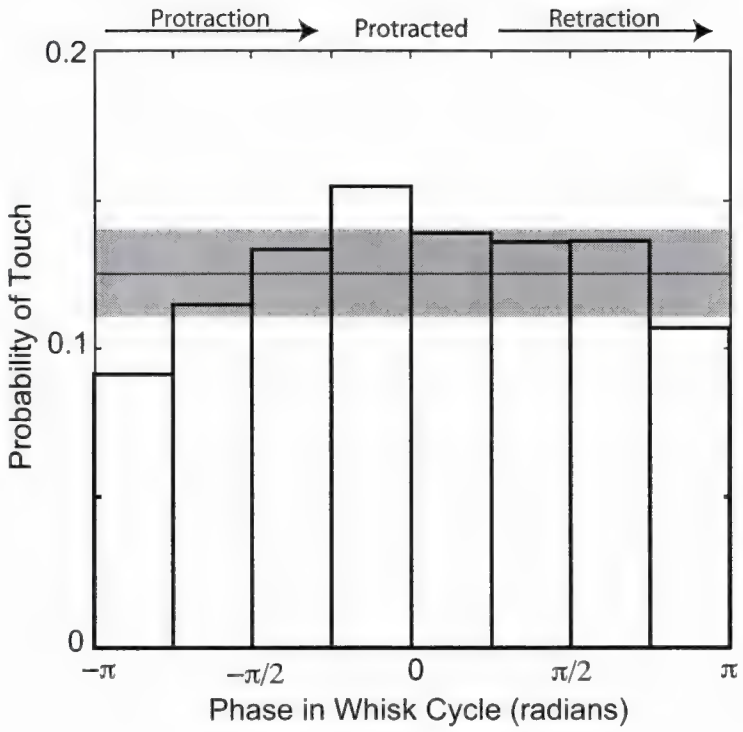
Coding object location in the vibrissa scanning sensorimotor system

Thank you for your attention!

Supplemental Material for NN-A26718-T
"Phase-to-rate transformations encode touch in cortical neurons of a scanning sensorimotor system" by John Curtis and David Kleinfeld

Figure S1. Overall distribution of whisk cycle phases of touch events for all units with rapid response to touch. Plot of the relative frequency of touch events at different phases of the whisk cycle. The blue horizontal line indicates the mean probability of touch over all phase intervals. The shaded region around this line indicates 95 % confidence limits for a uniform distribution. Although touch events near retraction are significantly less frequent, a sufficient number of these events occur in each session to produce stable touch response estimates, e.g., the mean number of touch events per session for the interval at the start of protraction (the lowest bar on the plot) is 12 touches per session. In general, each interval had at least 8 touches per individual session in the data sets that we analyzed.

Nature Neuroscience: doi:10.1038/nn.2283

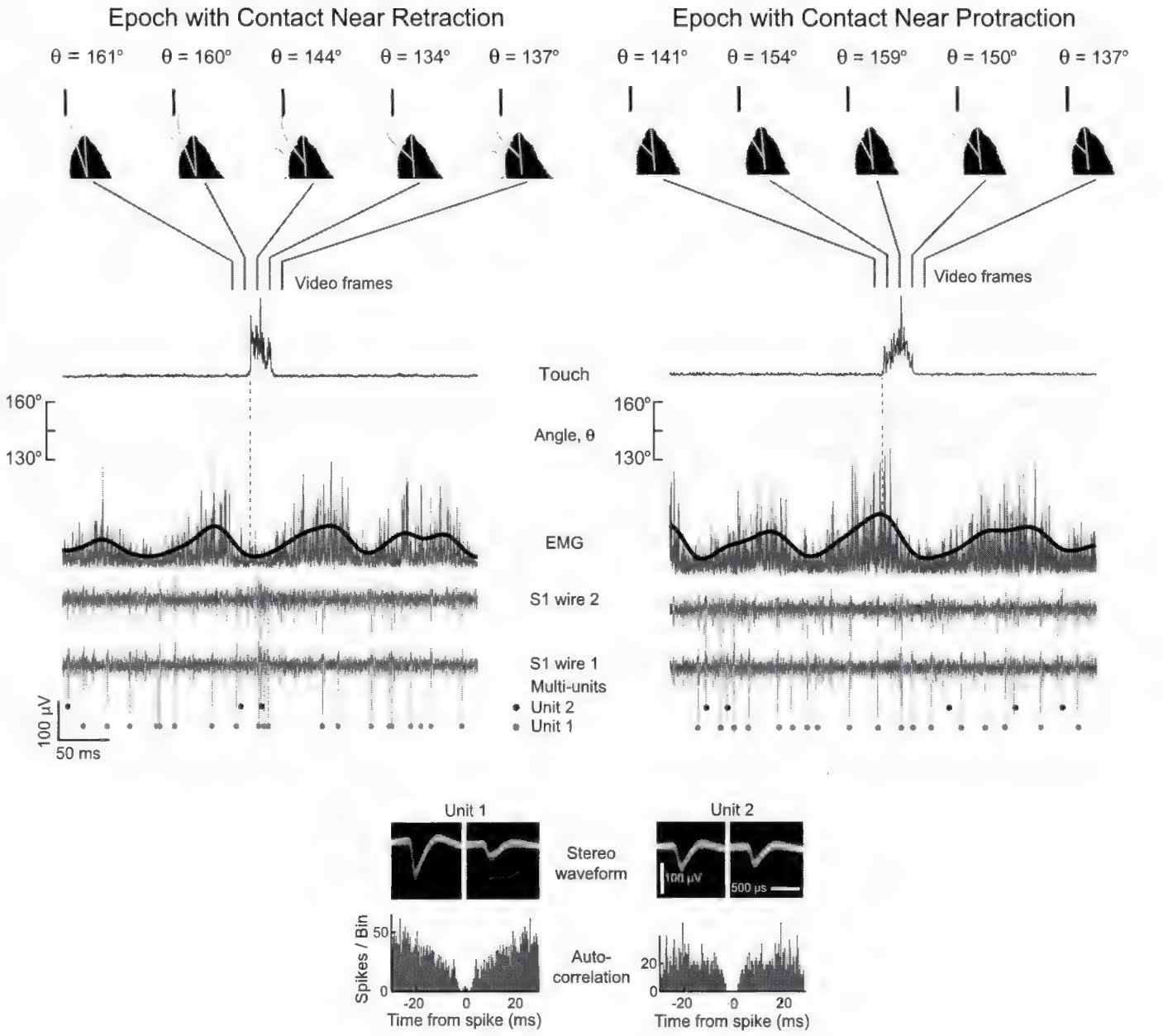


Nature Neuroscience: doi:10.1038/nn.2283

Figure S1 - Curtis and Kleinfeld

Supplemental Material for NN-A26718-T
"Phase-to-rate transformations encode touch in cortical neurons of a scanning sensorimotor system" by John Curtis and David Kleinfeld

Figure S2. Example of raw data for a unit with a touch response modulated by whisking. Plots of high speed video frames, videographic position signal, rectified touch sensor signal, rectified (and low pass filtered) EMG signal, and S1 cortex recording channels surrounding two touch events during a recording session. Dots indicate times of contact events and sorted spike times for two units (waveforms and autocorrelations are shown at the bottom). The left plots show the rat touching the sensor during retraction and touch in the right plots is during protraction. Unit 1 is rapidly excited by touch and Unit 2 does not respond to touch. The spike activity of Unit 1 is modulated by free whisking and its touch response is modulated by whisking. The preferred phases of free whisking and touch for Unit 1 are near retraction, i.e., $\phi_{whsik} = 0.84\ \pi$ for whisking and $\phi_{touch} = 0.82\pi$ for touch. The touch event to the left is within the preferred phase of Unit 1 as can be seen by increased spiking briefly after touch is initiated. The touch event to the right occurs nearly opposite to the preferred phase of Unit 1 and spiking briefly after touch remains similar to background activity.

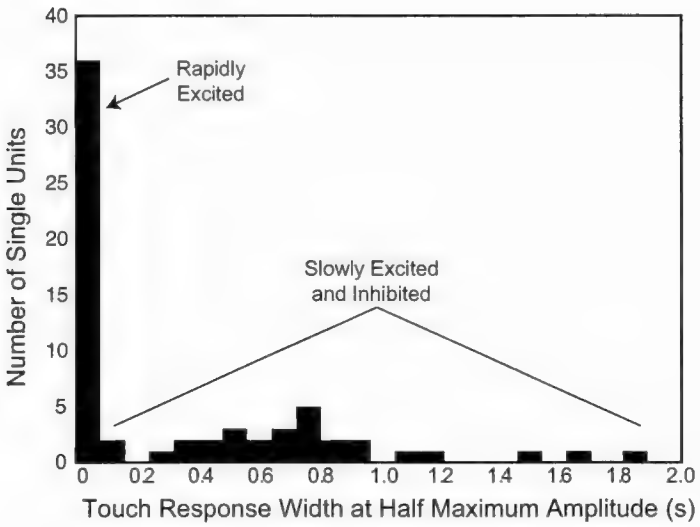


Nature Neuroscience: doi:10.1038/nn.2283

Figure S2 - Curtis and Kleinfeld

Supplemental Material for NN-A26718-T
"Phase-to-rate transformations encode touch in cortical neurons of a scanning sensorimotor system" by John Curtis and David Kleinfeld

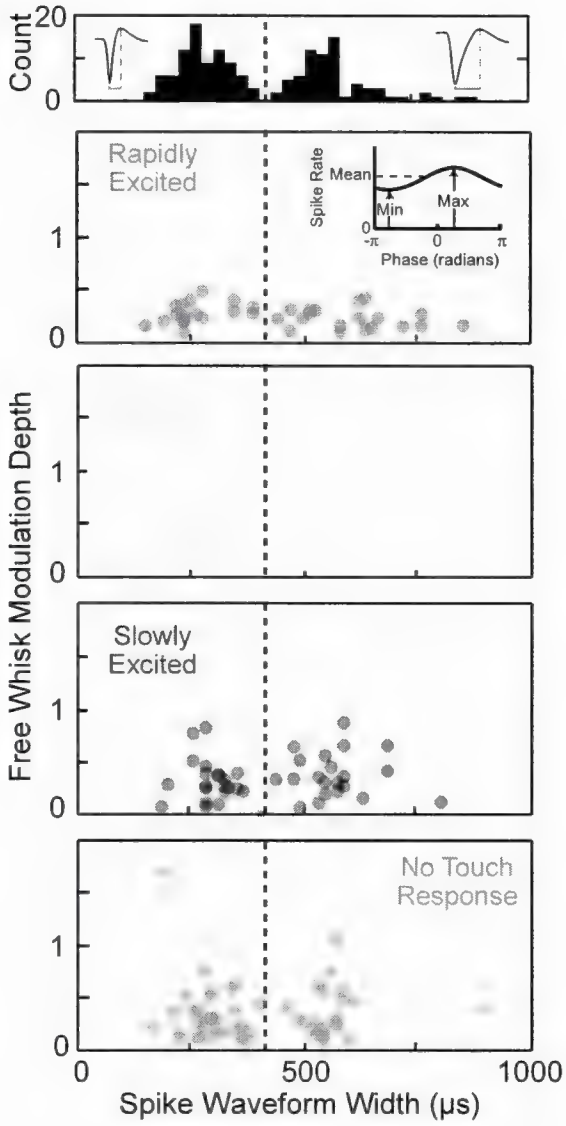
Figure S3. Distribution of touch response widths. Histogram of the width of the response to touch (full width at half maximum amplitude) for all excited or inhibited touch responses, *i.e.*, rapid excited, slow excited, and slow inhibited. Units with no response to touch are not included. Note that all rapid excited touch response widths fall within the first bin of the plot.



Nature Neuroscience: doi:10.1038/nn.2283

Figure S3 - Curtis and Kleinfeld

Figure S4. Free whisking modulation depths and spike waveform widths for all units according to touch response type. **(Top)** The distribution of different classes of single units according to the width, measured from peak to trough, of the waveform for the unit. The inserts show typical waveforms. **(Lower)** Free whisking modulation depth, measured from minimum to maximum divided by mean spike rates, plotted as functions of spike waveform width for the three difference responses, i.e., rapid excited, slow excited, and slow inhibited, as well as unresponsive cells.



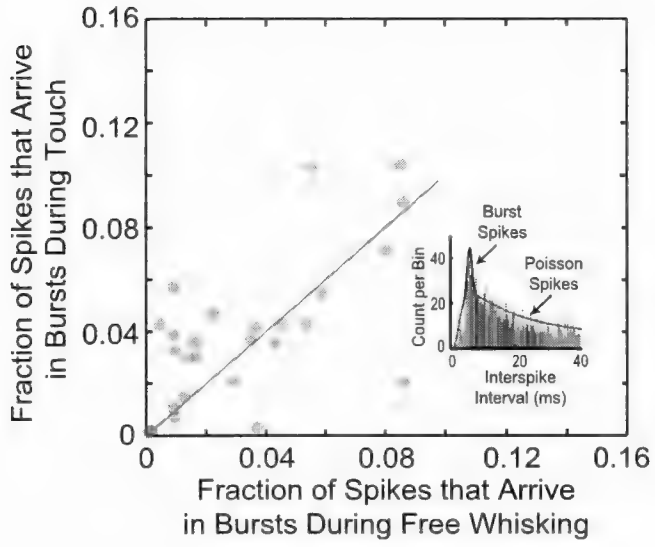
Nature Neuroscience: doi:10.1038/nn.2283

Figure S4 - Curtis and Kleinfeld

Supplemental Material for NN-A26718-T
"Phase-to-rate transformations encode touch in cortical neurons of a scanning sensorimotor system" by John Curtis and David Kleinfeld

Figure S5. Probability of burst generation by single units in S1 vibrissa cortex. To quantify bursting activity in neurons excited by touch as opposed to free whisking in air, we produced separate interspike interval (ISI) histograms (bin width < 0.5 ms) for spikes that occurred during touch versus free whisking trials. To model normal spike activity, we used a generic form of the Inverse Gaussian equation to capture the refractory period spiking and exponential decay in number of ISI's at higher values. Bursting activity was modeled as a Gaussian function where the center and width were chosen manually such that the function was confined to the relative refractory period. If a particular ISI histogram contained a distinct peak at small values, which is indicative of bursting, the center and width of the Gaussian function were adjusted to best fit the peak. Functions were fit to the ISI histograms using Poisson distributed maximum likelihood estimates. Since particular ISI distributions were modeled as a linear combination of the Gaussian and Inverse Gaussian functions, the number of ISI values contributed by each could be calculated separately. Thus the number of ISI values that resulted from bursting was calculated by taking the difference in number of ISI values between the Gaussian and Inverse Gaussian fitted curves (bursting and normal spiking) and the Inverse Gaussian fitted curve (normal spiking only). The number of ISI values due to bursting was then divided by the total number of ISI values in order to compare the relative amount of bursting among different ISI distributions, i.e., between free whisking and touch trials of the same neuron as well as among different neurons.

Nature Neuroscience: doi:10.1038/nn.2283

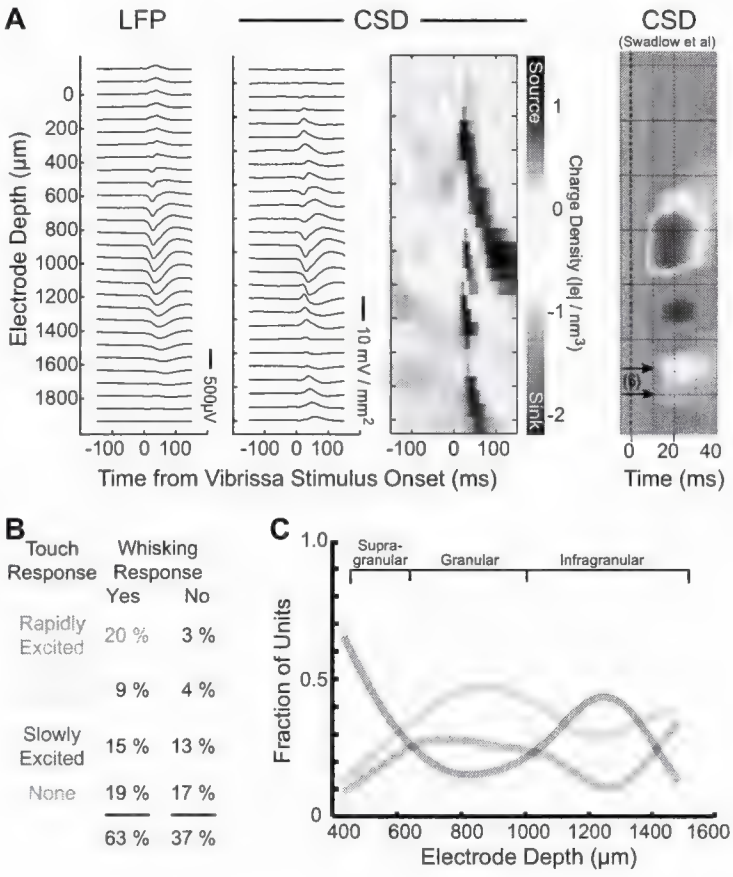


Nature Neuroscience: doi:10.1038/nn.2283

Figure S5 - Curtis and Kleinfeld

Supplemental Material for NN-A26718-T
"Phase-to-rate transformations encode touch in cortical neurons of a scanning sensorimotor system" by John Curtis and David Kleinfeld

Figure S6. Laminar distribution and spike widths of different classes of single units. **(A)** Representative local field potential (LFP) measurements along with the current source density (CSD) calculated from these measurements. The CSD, shown also in false color to emphasize sinks and sources of current, was used to classify the cortical layer and depth for each recording. The plot on the right confirms that at least the short-time measurements concur with the past results of Swadlow, Gusev and Bezdudnaya (Activation of a cortical column by a thalamocortical impulse. 2002. J Neurosci 22, 7766-7779). **(B)** Compendium of responses across all single-units. **(C)** The laminar distribution of single-units that responded to active touch, independent of their whisking related response.

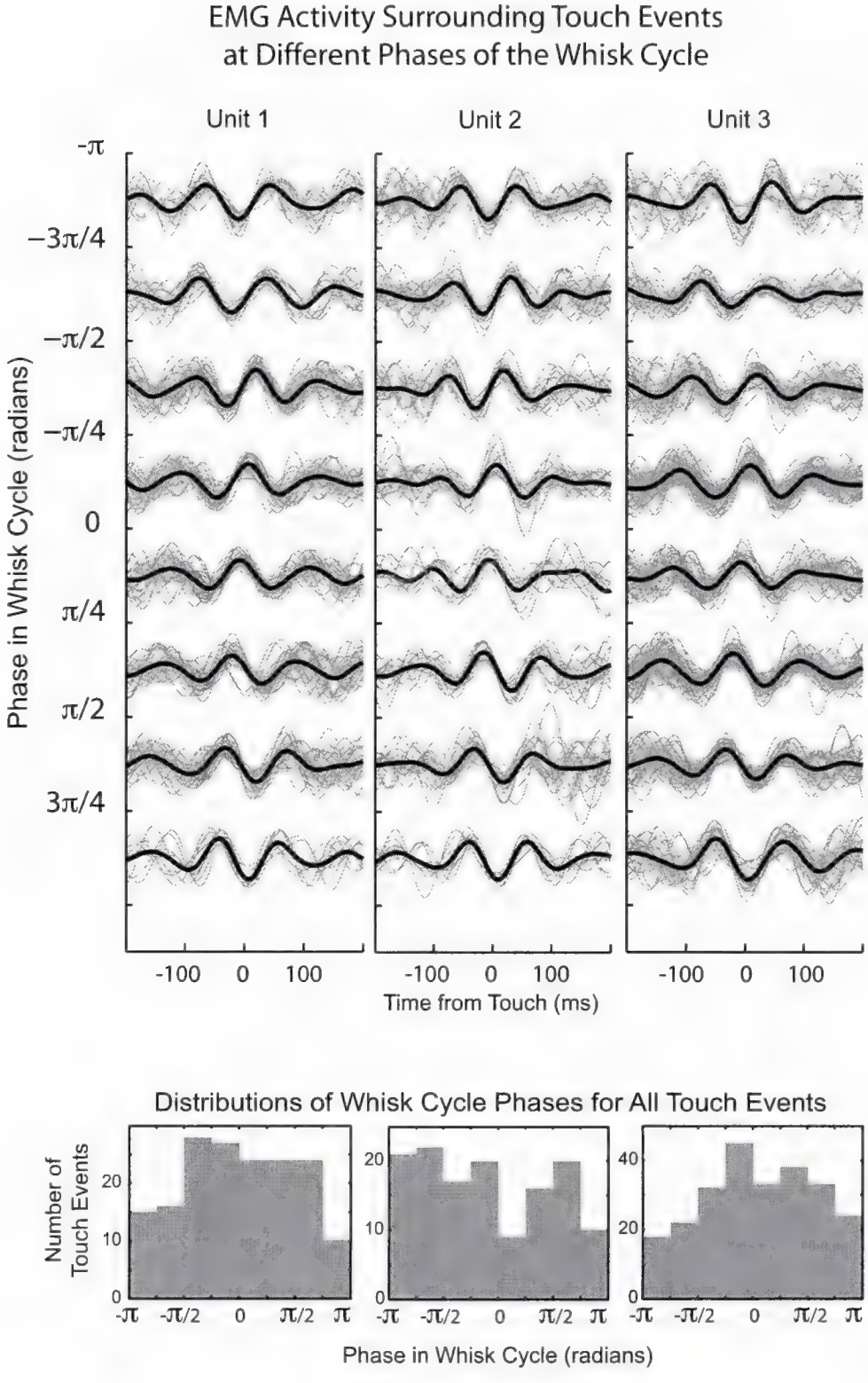


Nature Neuroscience: doi:10.1038/nn.2283

Figure S6 - Curtis and Kleinfeld

Supplemental Material for NN-A26718-T
"Phase-to-rate transformations encode touch in cortical neurons of a scanning sensorimotor system" by John Curtis and David Kleinfeld

Figure S7. Examples of whisking activity that surrounds touch events. Each plot shows whisking activity that surrounds touch events that are sorted by where touch occurs in the whisk cycle. The data applies to the three units included in figure 4. Single whisking trajectories are thin lines overlaid in grey and mean trajectories are thick black lines. The lower plots show the relative frequencies of touch at different whisk cycle phases for each unit's recording session.



Nature Neuroscience: doi:10.1038/nn.2283

Figure S7 - Curtis and Kleinfeld

Figure S8. Free whisking and touch responses for all units with rapid response to touch that are significantly modulated by phase in the whisk cycle. Autocorrelations and waveforms for each neuron are plotted at the right end of each row. **(A1–A4).** Average spike response histograms in response to free whisking centered on ∇EMG peaks with sinusoid fits (green lines) and resultant parameters, i.e., DC = average spike rate across histograms, Amp = amplitude of sinusoid fit (DC to peak), ϕ = preferred phase, mod = response modulation depth. **(B1–B4)** Average spike responses to touch with BARS fits (green lines). Peak and baseline rates calculated from smooth curve are listed above each plot. **(C1–C4)** Left: Average touch response histograms parsed by phase in the whisk cycle using ∇EMG data to determine the phase. Right: Plots of the peak values of the touch response from fits to each of the eight intervals of the smooth curve touch responses in the left hand panels. The parameters listed above each plot were estimated by fitting a sinusoid to each curve and have the same designation as in panel A. Dotted lines indicate 95 % confidence intervals for mean spike rate estimates. **(D1–D4)** Left: Average touch response histograms parsed by phase in the whisk cycle using videographic data to determine the phase. Right: Plots of the peak values of the touch response from fits to each of the eight intervals of the smooth curve touch responses in the left hand panels. **(E1–E4)** Left: Average touch response histograms parsed by speed in the whisk cycle using videographic data to determine the speed. Right: Plots of the peak values of the touch response from GLM fits to each of the eight intervals of the smoothed touch responses in the left hand panels. **(F1–F4)** Left: Average touch response histograms parsed by angular position in the whisk cycle using videographic data to determine the position. Right: Plots of the peak values of the touch response from GLM fits to each of the eight intervals of the smoothed touch responses in the left hand panels.

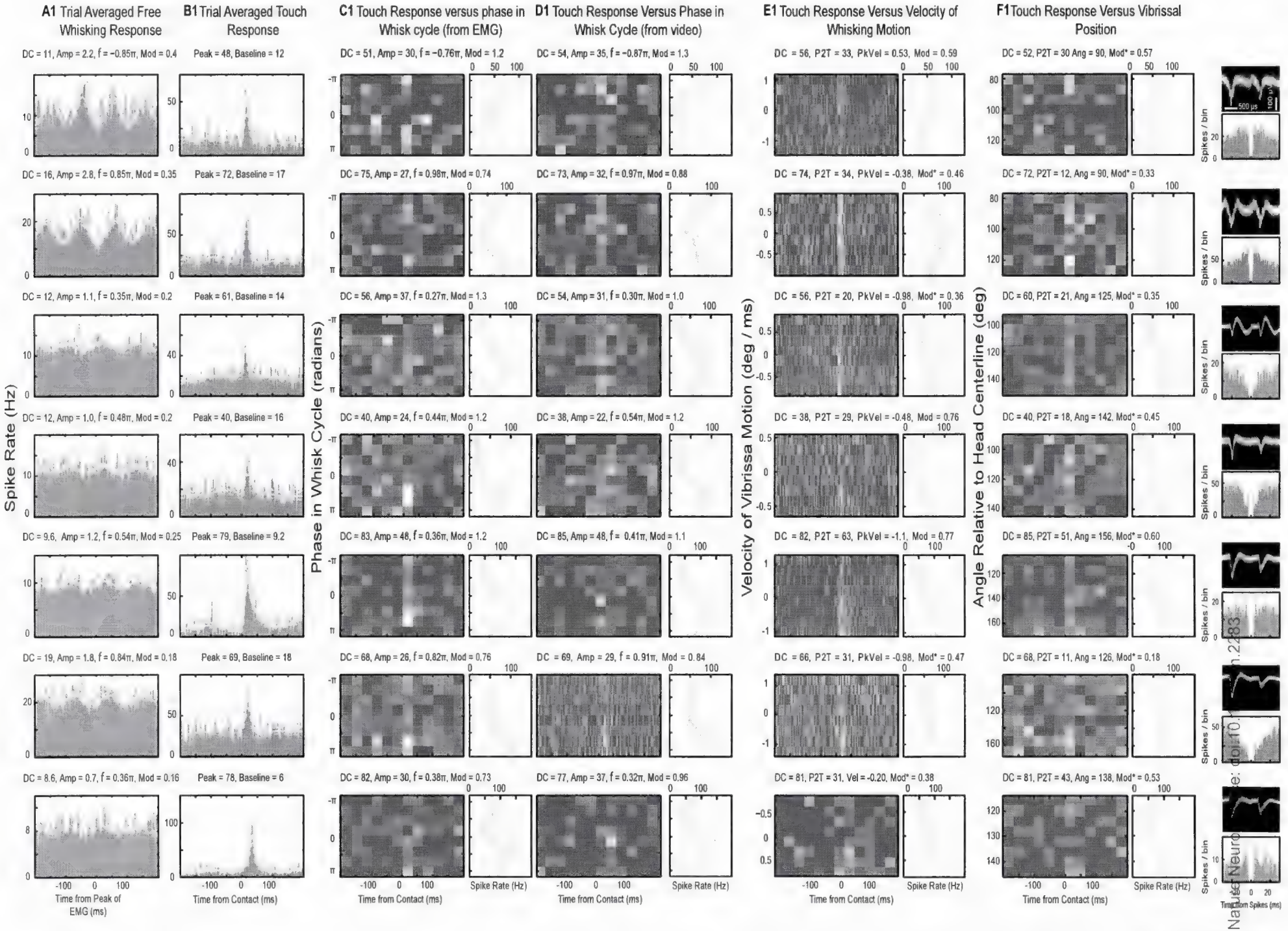


Figure S8 (1-7) - Curtis and Kleinfeld

Nature Neuroscience: doi:10.1038/nn.2283

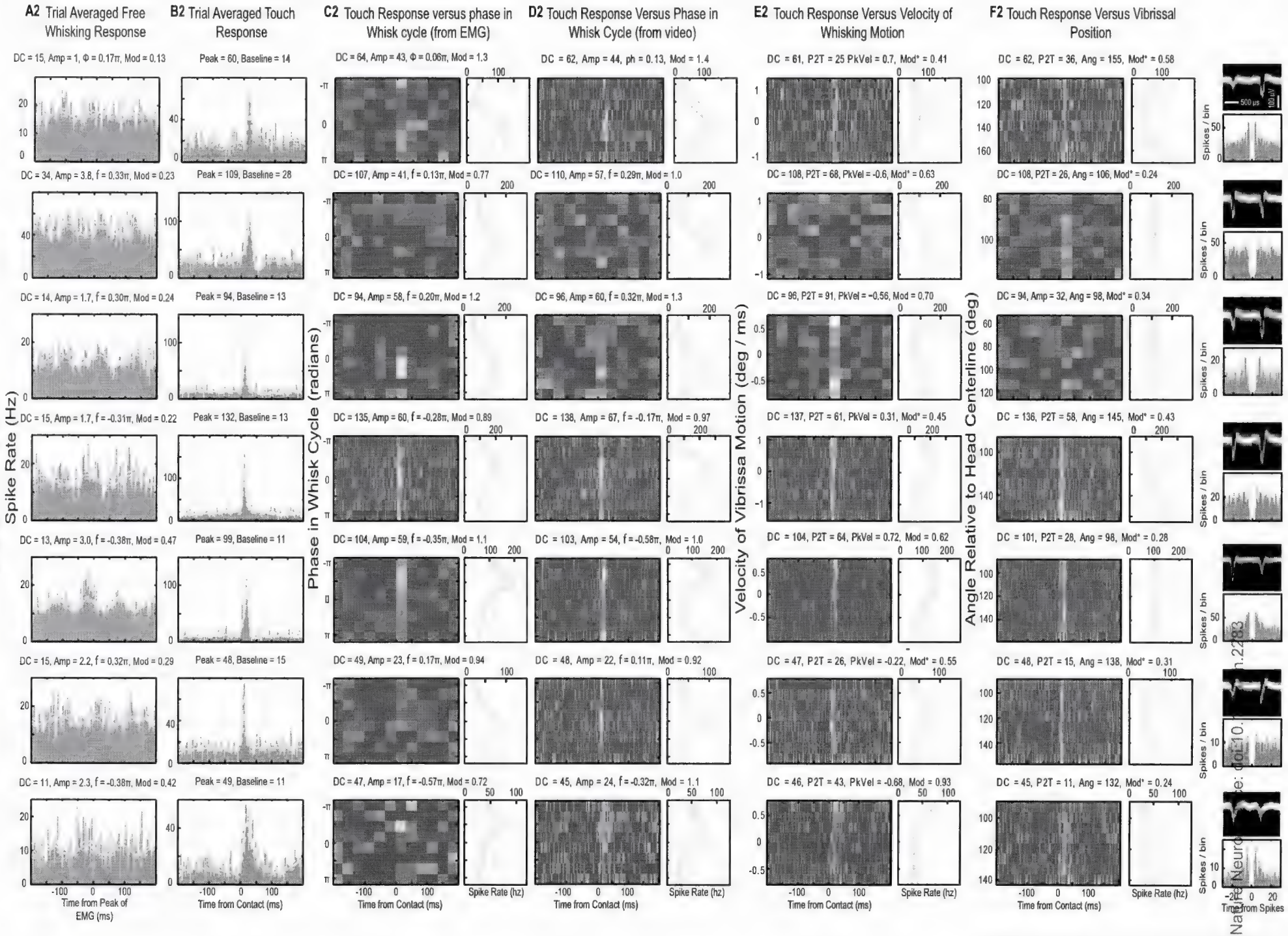


Figure S8 (8-14) - Curtis and Kleinfeld

Nature Neuroscience: doi:10.1038/nn.2283

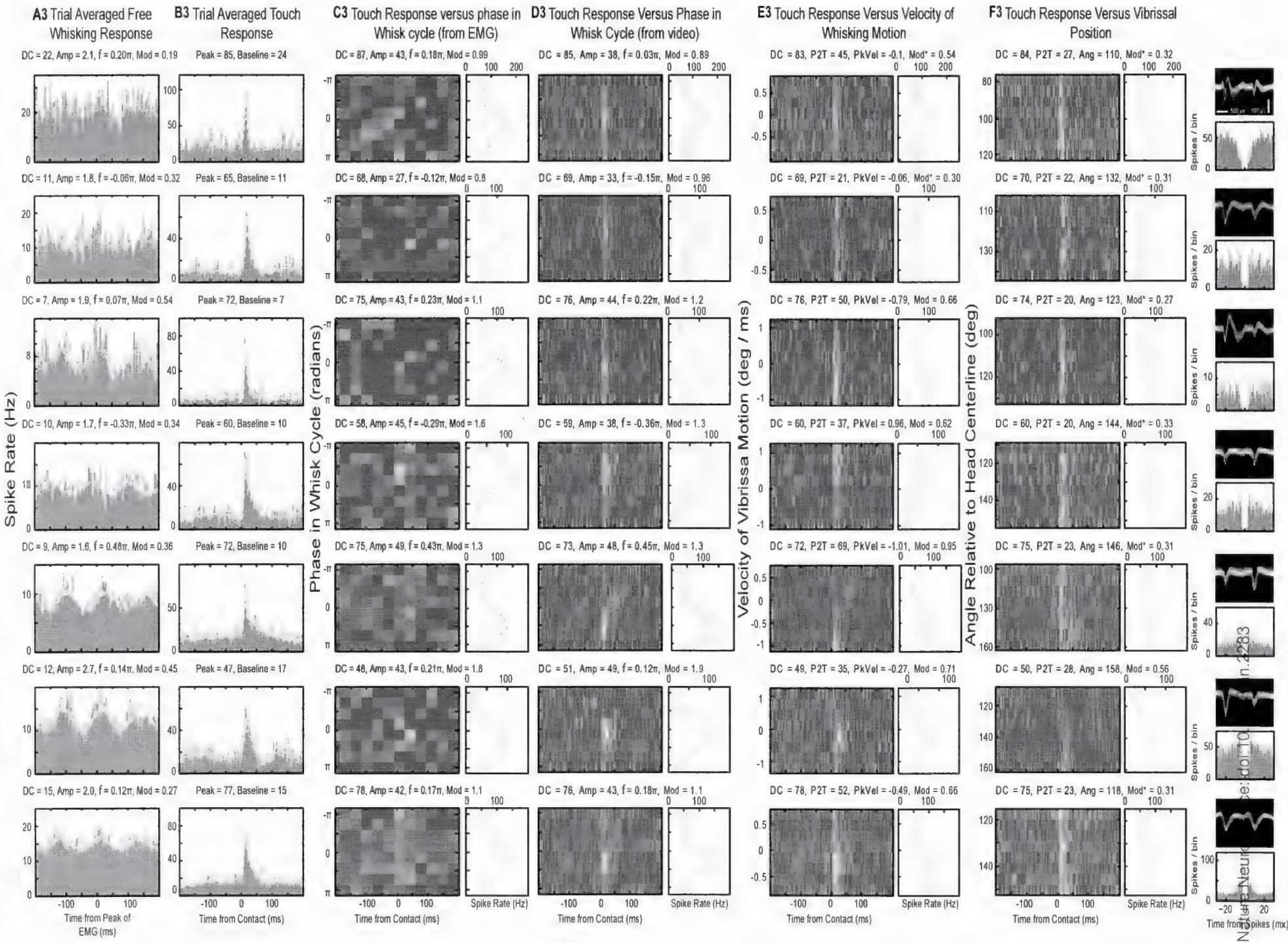


Figure S8 (15-21) - Curtis and Kleinfeld

Nature Neuroscience: doi:10.1038/nn.2283

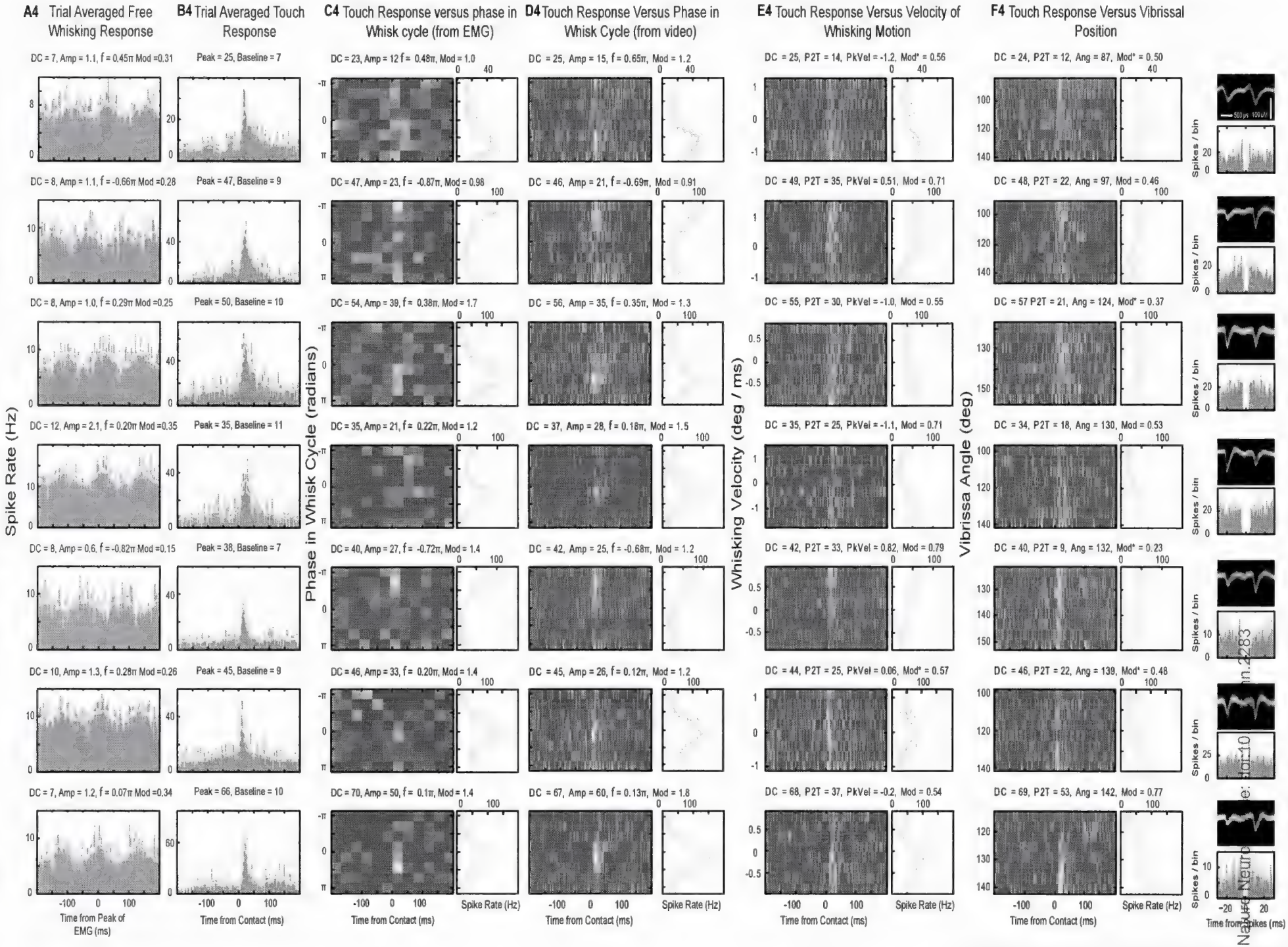


Figure S8 (22-28) - Curtis and Kleinfeld

Nature Neuroscience: doi:10.1038/nn.2283

Supplemental Material for NN-A26718-T
"Phase-to-rate transformations encode touch in cortical neurons of a scanning sensorimotor system" by John Curtis and David Kleinfeld

Figure S9. Free whisking and touch responses for all units with rapid response to touch that are not modulated by phase in the whisk cycle. **(A).** Average spike response histograms in response to free whisking centered on EMG peaks with sinusoid fits (green lines) and resultant parameters defined in caption for figure S8. An asterisk denotes insignificant fit. **(B)** Average spike responses to touch with BARS fits (green lines). Peak and baseline rates calculated from smooth curve are listed above each plot. **(C)** Average touch response histograms parsed by phase in the whisk cycle. **(D)** Plots of the peak values of the touch response from fits to each of the eight intervals of the smooth curve touch responses in panel C. The parameters listed above each plot were estimated by fitting a sinusoid to each curve and have the same designation as in panel A. Dotted lines indicate 95 % confidence intervals for mean spike rate estimates. **(E)** Autocorrelations and waveforms for each neuron.

Nature Neuroscience: doi:10.1038/nn.2283

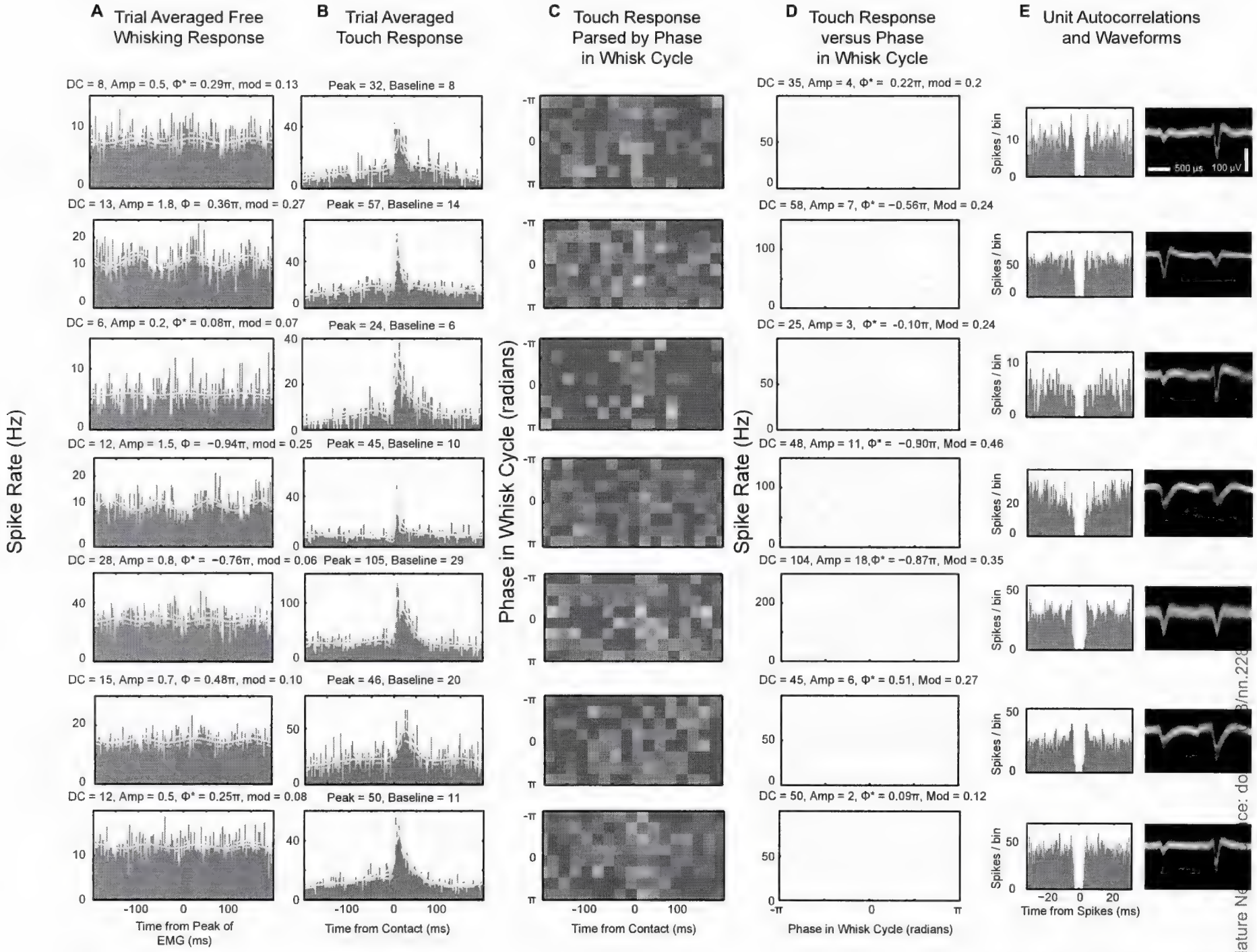
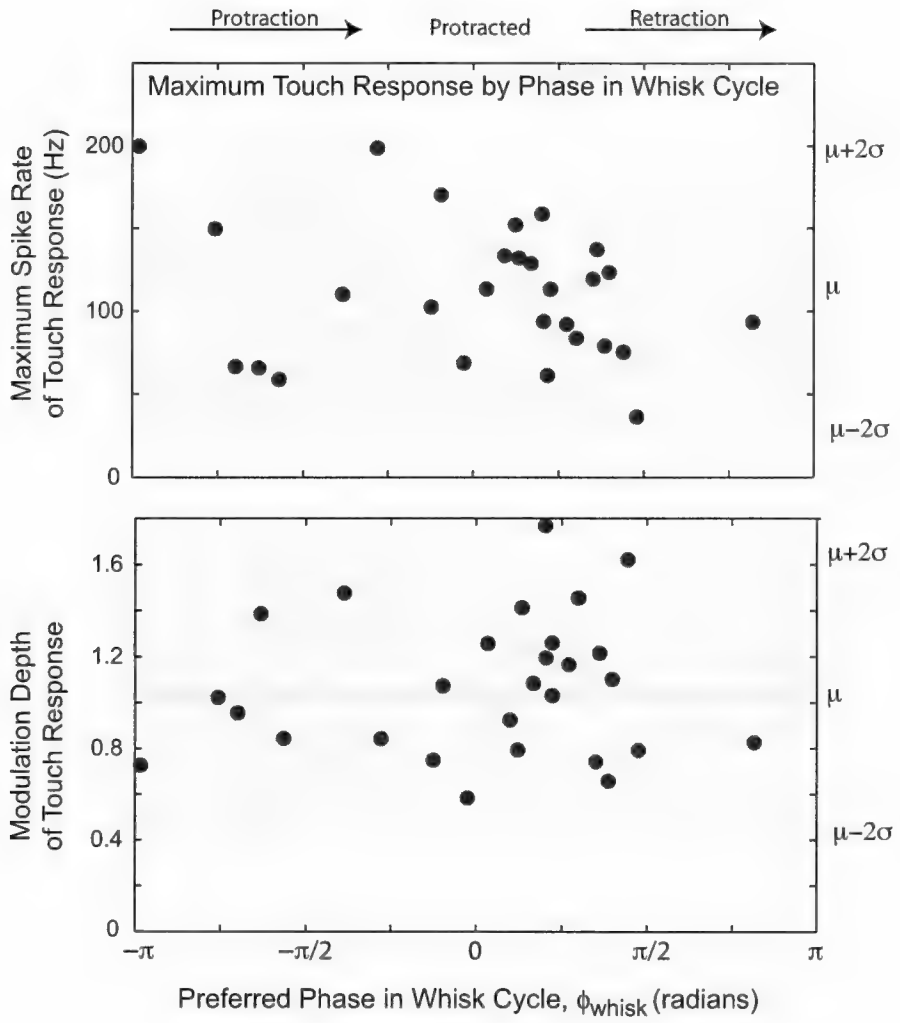


Figure S9 - Curtis and Kleinfeld

Nature Neuroscience: doi:10.1038/nn.2281

Figure S10. Comparisons of maximum touch response and modulation depth at different preferred phases. **(A)** The spike rate for the maximum touch response as a function of preferred phase for units with whisking modulated rapid touch responses. **(B)** The modulation depth of the touch response plotted as a function of each unit's preferred phase. Mean values across all preferred phases are indicated in each plot by dark green line along with 95 % confidence band in light green. There is no significant tendency for either maximum touch response amplitude or modulation depth to be greater at any specific preferred phase relative to other preferred phases.



Nature Neuroscience: doi:10.1038/nn.2283

Figure S10 - Curtis and Kleinfeld

Supplemental Material for NN-A26718-T
"Phase-to-rate transformations encode touch in cortical neurons of a scanning sensorimotor system" by John Curtis and David Kleinfeld

Figure S11. The preferred phase in the whisk cycle for contact estimated from ∇EMG data versus videographic data. The slope of the best fit line is 0.92 ($p < 0.001$).

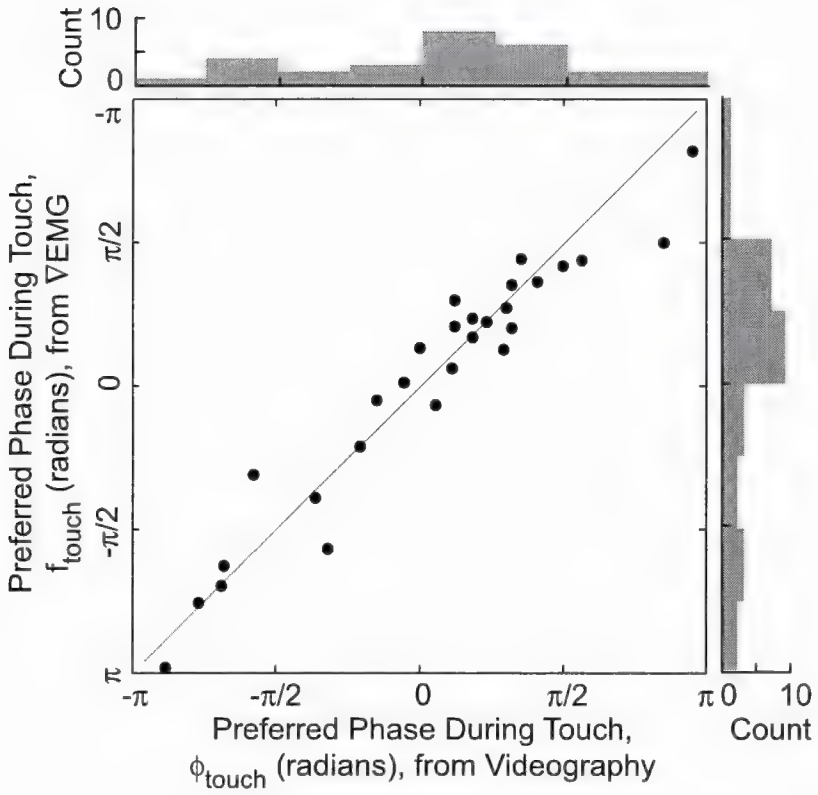


Figure S11 - Curtis and Kleinfeld

Nature Neuroscience: doi:10.1038/nn.2283

Supplemental Material for NN-A26718-T
"Phase-to-rate transformations encode touch in cortical neurons of a scanning sensorimotor system" by John Curtis and David Kleinfeld

Figure S12. Touch responses as a function of phase in the whisk cycle for changes in whisking parameters. Shown are examples, including that for unit 3 shown in figure 6 of the main text.

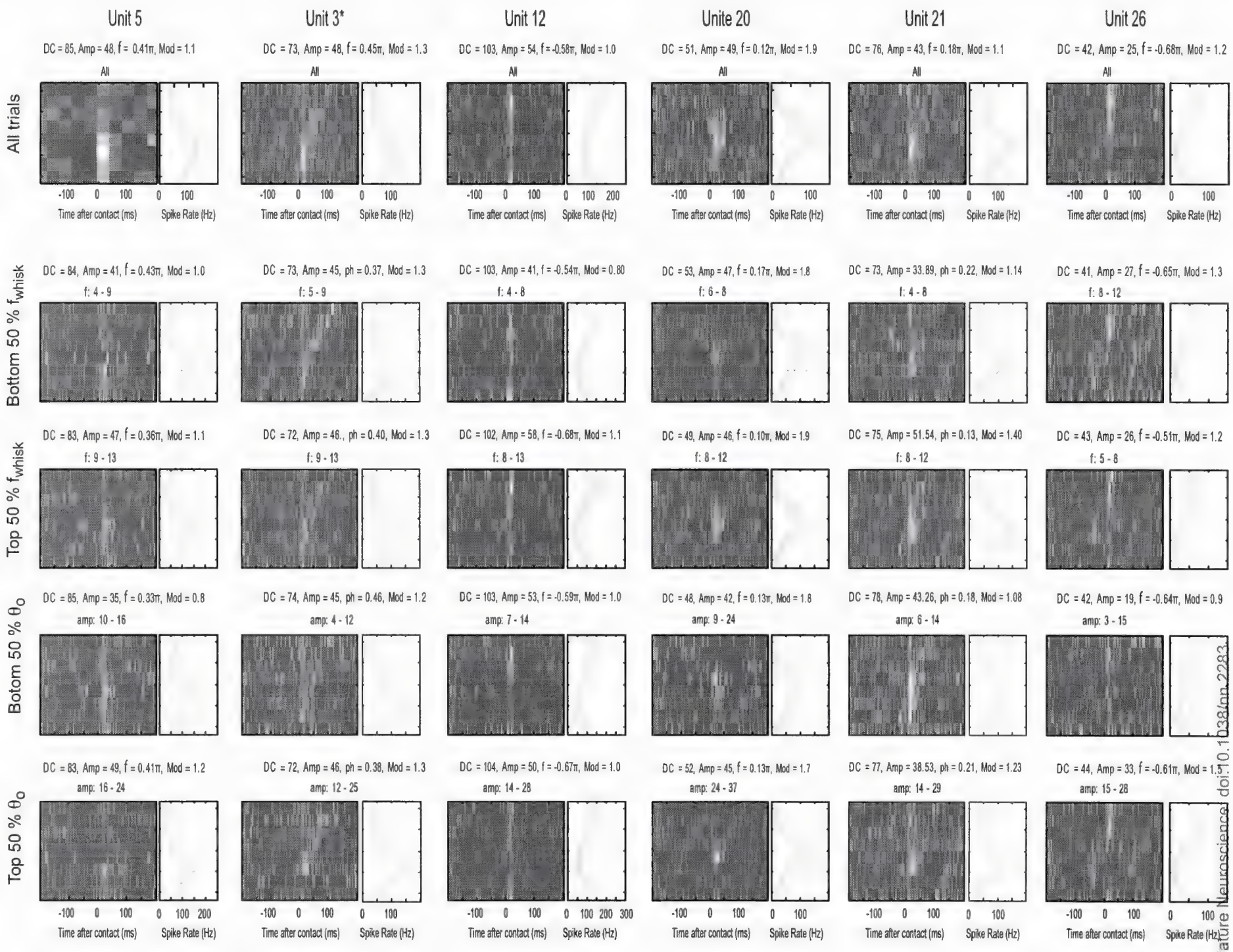


Figure S12 - Curtis and Kleinfeld

Nature Neuroscience doi:10.1038/nn.2283

NRSC: 01351

a0005

Vibrissa Movement, Sensation and Sensorimotor Control

D Kleinfeld, University of California, San Diego, La Jolla, CA, USA

© 2008 Elsevier Ltd. All rights reserved.

s0005

Introduction

p0005 Rats use their vibrissae, an array of long, pliable hairs that can be actively swept through space, to interrogate objects in their local physical environment (**Figures 1(a)** and **1(b)**). As rats search and locomote, they must be able to gauge the position of the ground beneath them and walls and obstacles around them. This suggests that the sense of touch is used in multiple ways. First, touch provides a means to establish the nature of a surface texture. Is it smooth or rough? Second, touch is used to establish the shape of an object. Third, touch is used as a means to determine the location of an object with respect to the body image of the rat. Is the object to the front or the side? The notion of interpreting touch in the context of body coordinates implies that reference signals of vibrissa position are an essential aspect of sensation.

p0010 The neuronal encoding of environmental and positional clues, and the anatomical circuitry that turns these clues into motor plans, form the material of this article. It begins by delineating a number of tasks that rats may be trained to accomplish solely through the use of their vibrissae. These serve to focus our presentation on neuronal pathways that are directly relevant to an understanding of vibrissa sensorimotor control. The article then discusses the anatomy of the vibrissa pathway in detail, with an emphasis on the mechanical properties of the vibrissa *per se*, as well as the motor plant that drives the vibrissae. This leads into a presentation of electrical signaling along the vibrissa pathways, followed by consideration of the neuronal computations that are supported by these signals. The article closes with a discussion of open issues. As an aid to reading the literature, common abbreviations are given in **Table 1**.

s0010

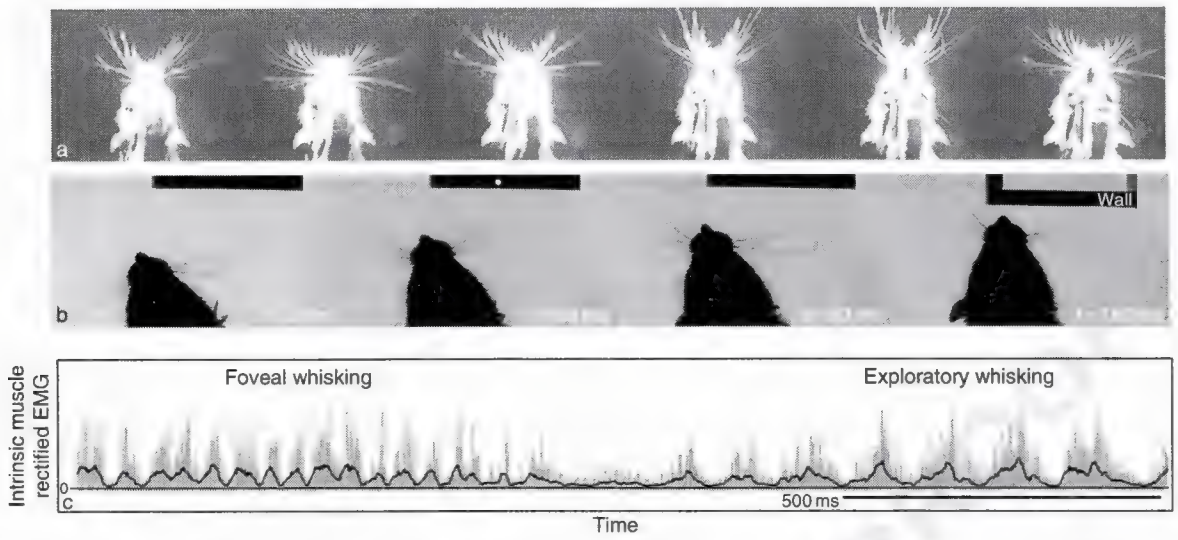
Behavior

p0015 Vibrissae somatosensation is an active sensory process. Rodents sweep their vibrissae through space largely in unison and with a rhythm that varies between 5 and 25 Hz. The dynamics of this process can be extracted from high-speed videography or from measurements of the electrical activity of the muscles that drive the vibrissae (**Figure 1(c)**). What tasks can animals accomplish with this active process? A basic function of the vibrissae is to evaluate the terrain in front of the animal. Thus, for example, blind rats with intact vibrissae will leap across wider gaps than rats without vibrissae. This observation is a building block of a commonly used paradigm to determine whether rats can discriminate among surfaces with different textures (**Figure 2**). Here, rats foveal whisk as they crane across each of two gaps (**Figure 1(c)**). This posture allows them to sense and evaluate a texture on the far side of the gap. Only one of the two textures is paired with a reward, that is, water or food, which the animal can receive by jumping across the gap. The accumulated data from these experiments suggest that trained animals may recognize a corrugated surface whose pitch is as fine as 15μm and differentiate among surfaces whose relative difference in pitch is as small as 5%. Last, these experiments reveal that the amplitude of whisking may change upon contact (**Figure 2(a)(2)**) and thus provides a means to manipulate sensorimotor feedback.

p0020 The vibrissae convey spatial information that is sufficient to allow rats to distinguish between barriers whose lateral distance from the snout varies by less than 5%. In one task, rats are trained to distinguish between a wide versus narrow aperture (**Figures 2(b)(1)** and **2(b)(2)**). A rat waits in a main chamber until a sliding door opens, after which it enters a small chamber that contains a nose poke, that is, a place for the snout that keeps the rat's head relatively fixed during the task. Once the snout is positioned, two panels close from the sides to form a symmetric, variable-width aperture. Animals are required to judge whether the aperture is the wider or narrower of two possible widths and report their choice by moving to additional nose pokes in the main chamber, that is, a right nose poke for the narrow aperture and a left nose poke for the wide aperture (**Figure 2(b)(1)**). The correct choice is rewarded. An interesting result is that, as the vibrissae are incrementally trimmed from the normal complement of 20 or more down to one and then zero, the performance on this task is a linearly decreasing function of the number of vibrissae that remain (**Figure 2(b)(2)**).

p0025 Variants of the above fine-discrimination task require the animal to report symmetric versus asymmetric apertures. In a related task, animals are trained to report the shift in the horizontal position between pins placed on each side of the face (**Figure 2(c)(1)**). This latter task probes the bilateral acuity of the vibrissa system. It is interesting that rats perform this task better with only a single column, referred to as arc, of vibrissae rather than all their vibrissae (**Figure 2(c)(2)**). The typical displacement that could be distinguished with an arc was 1.5 mm, which corresponds to an angular displacement of 6° in these experiments.

NRSC: 01351



f0005 **Figure 1** Example data for different modes of whisking. (a) Exploratory whisking, also referred to as symmetric whisking. Shown are successive strobed video images of a rat, using darkfield illumination, as it moves its vibrissae during an exploratory whisk cycle. The animal was trained, while blindfolded, to whisk in search of a food tube (not shown). Successive frames are at intervals of 33 ms. Unpublished data. (b) Asymmetric whisking as a result of contact between the vibrissae and a wall. Protraction commences approximately synchronously on both sides of the snout; the filled white squares show the tracked vibrissae in the rear arcs. At $t = 65$ ms, a deflection occurs on a forward vibrissa; the filled white circle indicates the point of contact with the vertical surface. Protraction then ends on the side ipsilateral to the contact, and the contralateral vibrissae reach maximum protraction in the whisk cycle subsequent to the initial contact. Adapted from Mitchinson B, Martin CJ, Grant RA, and Prescott TJ (2007) Feedback control in active sensing: Rat exploratory whisking is modulated by environmental contact. *Proceedings. Biological Sciences/The Royal Society* 274(1613): 1035–1041. A similar pattern of asymmetric whisking as animals change their head position has been reported by Hartmann (Towal RB and Hartmann MJ (2006) Right-left asymmetries in the whisking behavior of rats anticipate head movements. *Journal of Neuroscience* 26: 8838–8846). (c) Example of sequential foveal and exploratory whisking observed via the rectified electromyogram of the intrinsic muscles. The solid line is the low-pass filtered signal. Adapted from Berg RW and Kleinfeld D (2003) Rhythmic whisking by rat: Retraction as well as protraction of the vibrissae is under active muscular control. *Journal of Neurophysiology* 89: 104–117.

p0030 Beyond issues of discrimination, rats make use of vibrissa somatosensation to encode the location of objects relative to their face as they explore their environment with large-amplitude whisks (**Figure 1(a)**). In part, the ability of rats to use their vibrissae to sense a platform across a gap implies that they are sensitive both to touch and to the forward thrust of their vibrissae. Nonetheless, the question remains as to whether rodents encode the position of their vibrissae as they whisk (**Figure 3(a)**). This issue was addressed in terms of an operant conditioning paradigm in which rats were trained to discriminate between different angles of a pin relative to the area of the cheek that hosts the vibrissae, called the mystacial pad (**Figure 3(b)**). These animals were trained to press a lever at a high rate if the rewarded stimulus (S+), corresponding to a pin at a specified location, was presented. No reward occurred for a stimulus at a second location (S−). Rats with a single vibrissa were able to perform this task (**Figure 3(c)**). Further, they performed it without bias to vibrissa location and with few, relatively brief contacts. This implies that rats must make use of a reference signal of vibrissa position as they determine where touch occurs relative to their mystacial pad.

Whisking

s0015

Within laboratory settings, animals will typically whisk in bouts of five to 50 individual whisks with a continuum of behaviors. Nonetheless, three different motifs appear to be common. The first is exploratory whisking, which occurs when animals whisk in air without contact or with only light contact (**Figure 1(a)**). In this case the stroke on a given whisk approaches 70°, and a total field of up to 160° may be covered as the animal slowly shifts the set point of its whisk. Such whisking is extremely regular and typically occurs with a frequency between 7 and 12 Hz and a mean of 9 Hz. In particular, the bandwidth of exploratory whisking is at theoretical limits for a perfect oscillator, which implies that the motor drive may be described as a sinusoidal oscillation with a constant frequency.

p0035

The second whisking motif, asymmetric whisking, occurs when animals make contact with a large object, such as a wall, while they whisk (**Figure 1(b)**). It also occurs if they turn their head to the side while whisking. Asymmetric whisking lasts for only one to three whisk cycles. The final motif is referred to as foveal whisking and occurs when animals thrust all their

p0040

NRSC: 01351

t0005 **Table 1** Common abbreviations

Abbreviation	*Meaning*
ALBSF	Anterior lateral barrel subfield, a region of parietal cortex
CPG	Central pattern generator
EMG	Electromyogram
FN	Facial nucleus
ICMS	Intracortical microstimulations
IoN	Infraorbital branch of the trigeminal nerve
L1, ..., L6	Neocortical layer 1, ..., layer 6
LFP	Local field potential
M1	Primary motor region of neocortex
MUA	Multiunit activity
PMBSF	Posterior medial barrel subfield, a region of parietal cortex
PO	Posterior medial nucleus, a region of dorsal thalamus (also POm)
PrV	Trigeminal nucleus principalis
RSU	Regular spiking unit
S1	Primary somatosensory region of neocortex (also SI)
S2	Secondary somatosensory region of neocortex (also SII)
SpVC	Spinal nucleus caudalis
SpVI	Spinal nucleus interpolaris
SpVO	Spinal nucleus oralis
TCU	Thalamocortical unit
TG	Trigeminal ganglion
TN	Trigeminal nucleus
VMCtx	Vibrissa primary motor cortex
VPM	Ventral posterior medial nucleus, a region of dorsal thalamus
VL	Ventral lateral nucleus, a region of dorsal thalamus
ZI	Zona incerta, a region of ventral thalamus

vibrissae forward to palpate an object ahead of them, as occurs when they try to detect a landing on the far side of a gap (**Figure 2(a)**). In this case the stroke is much reduced, typically to 20°, and the extrinsic muscles, the muscles that pull on the mystacial pad and include *m. nasolabialis*, *m. maxolabialis*, *m. nasalis*, and *m. transversus nasi*, are relatively inactive as they can apply little torque when the mystacial pad is fully extended. The frequency of foveal whisking is high, ranging between 15 and 25 Hz, and rats can readily switch between foveal and exploratory whisking (**Figure 1(c)**).

s0020 ## Systems Description of the Sensorimotor Plant

p0045 The anatomy of the vibrissa system provides the foundation for understanding the neuronal basis of whisking and vibrissa-driven behaviors. Like other sensorimotor systems, the vibrissa system is organized as a set of nested loops, with the vibrissae and the motor plant that drives the vibrissae as the common focus of all loops (**Figure 4**). The ascending branches of the loop receive and process sensory input, and the descending branches can control the motor plant that drives the vibrissae. It is important to remember that, as a closed feedback system, both sensory and motor signals can appear at all levels and stages of the nervous system. Only in extreme cases, such as induced paralysis of an identified pathway, can one isolate a touch signal from a motion signal that leads to touch.

The Follicle

s0025

p0050 The front end of the vibrissa system is the vibrissa–follicle complex (**Figure 5**). The lower 4 mm of the vibrissa is buried in the follicle, which is innervated by two sets of trigeminal sensory nerve terminals that originate from the trigeminal nucleus. One set innervates the deep end of the follicle (DVN in **Figure 5**) and the other innervates the superficial end (SVN in **Figure 5**). Together, these nerve fibers form the infraorbital branch of the trigeminal nerve (IoN).

p0055 The sensory nerves contain eight morphologically distinct sensory terminals, for which two classes of responses appear to dominate. One is the rapidly adapting receptors, whose responses return to baseline within 200 ms of stimulation, and the other is the slowly adapting receptors, which enable the vibrissa to follow vibrations as fast as 1200 Hz over extended periods. The latter responses are believed to make use of small cells called Merkel cells, localized to the follicle as intermediates between the hair and the sensory nerve terminal. The follicles, although composed exclusively of soft tissue, contain cavities that are under the control of the autonomic nervous system and engorge with blood when the animal is active. This results in a fixture that is likely to form a stiff mechanical coupling between the vibrissa and the sensory nerve terminals.

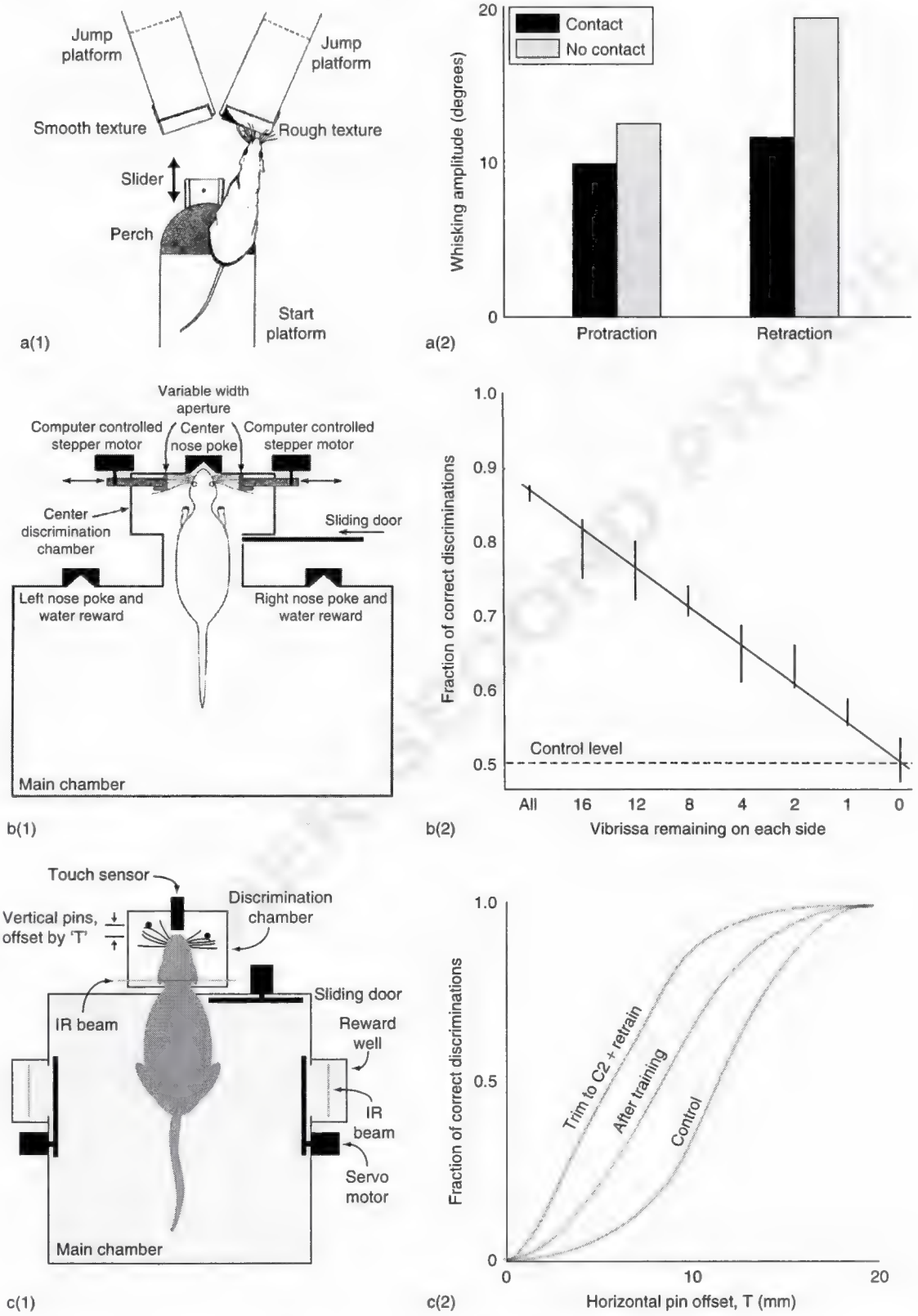
p0060 The sensory fibers in the follicle are sensitive to motion of the embedded vibrissa and thus encode contact between an object and the vibrissa. More information is gleaned if the impact on contact and the distance of the contact point to the skin, that is, the radial distance along the vibrissa, can be encoded. One likely possibility is that the reaction forces along the follicle shift as the point of impact moves relative to the center of mass of the vibrissa. Thus the pattern of these forces can be used to gauge the magnitude, distance, and direction of impact.

The Mystacial Pad

s0030

p0065 The cheek on each side of the rat's face contains a thickening in the skin that is called the mystacial pad. The pad contains an array of follicles organized as five rows and four or more arcs. In addition, there are

NRSC: 01351



f0010 **Figure 2** Behaviors that involve fine vibrissa-based comparisons. (a)(1) Schematic of a gap-crossing task in which rats crane across one of two equally spaced gaps to assess the relative roughness of textured tubes. Animals are trained to examine both textures and then jump from the perch on the start platform to the appropriate jump platform. The gap between the start and jump platforms can be adjusted

NRSC: 01351

four additional large caudal vibrissae, denoted the straddlers, which interdigitate among the rows (insert, Figure 5). The hairs in the most dorsal row, that is, row A, point upward above the head and, curiously, are barbered as animals determine dominance. The hairs in the ventral row, that is, row E, tap the ground as the animal locomotes and presumably help maintain the altitude of the head. The middle rows, labeled B through D, appear important to exploration and the location of objects.

s0035 **Brain Stem Loop**

p0070 Sensory input from reaction forces generated in the follicles leads to a signal that transverses the IoN and projects to one or all four nuclei that form the trigeminal complex (Figure 4). These include the principal sensory nucleus (PrV) and the three spinal nuclei, denoted oralis (SpVO), interpolaris (SpVI), and caudalis (SpVC). The afferents form several somatotopic representations, referred to as barrelettes, of the ipsilateral vibrissae. Efferents from the PrV, SpVC, and SpVI nuclei project to motor neurons in the lateral subnucleus of the ipsilateral facial nucleus, which sends motor output to the muscles of the mystacial pad. This completes the lowest-order brain stem sensorimotor loop (* in Figure 4).

p0000 The trigeminal nuclei further interact among each other. Neurons in the PrV nucleus receive excitatory input from both the SpVC and SpVI nuclei and inhibitory input from the SpVi nucleus. The latter forms a local inhibitory loop that, possibly in concert with descending inputs from high-order areas, provides a means to filter sensory information at the level of the brain stem.

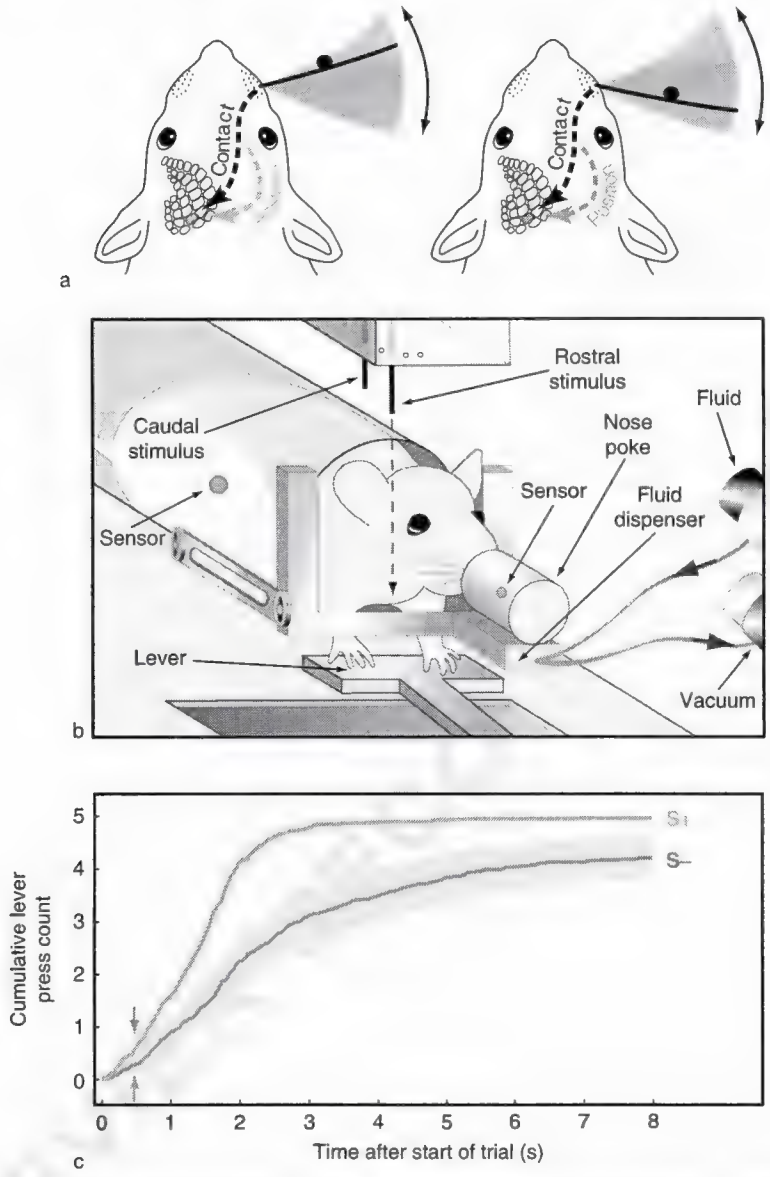
Muscles of the Mystacial Pad s0040

What is the underlying musculature that drives the vibrissae? Protraction begins with contraction of the external protractor muscles in the skin, m. nasalis (Figure 6(a)). This shifts the center of mass of the follicle, as well as the point of egress of the vibrissae, toward the snout. A second group of muscles, which appear as slings that wrap around each follicle, contract next and rapidly propel the vibrissae forward. These muscles are unique to animals that whisk and are denoted the intrinsic muscles (Figure 6(b)). Last, as protraction reaches its maximum extent, activation of the sling muscles wanes and a pair of external retractor muscles, m. nasolabialis and m. maxolabialis, activate and restore the vibrissae to their initial position (Figure 6(a)). The measured sequence of muscle activation, together with the measured motion of the vibrissae along an anterior–posterior (A–P) axis, illustrates this process (Figure 6(c)). Last, it is possible to construct a mechanical model of the mystacial pad that is based on the known anatomy, elastic constants of the tissue, and force curves for the muscles (Figure 6(d)). The model serves as a means to reconstruct the position of the vibrissae from the measured electrical activation of the vibrissae. p0075

Of critical importance, exploratory whisking occurs in the absence of sensory feedback. Moreover, the phase relation between the various muscle groups that mediate whisking is unchanged. This suggests the existence of coupled central pattern generators in the brain stem that drive the three phases of rhythmic whisking (Figure 6(c)). p0080

with a slider to change the difficulty of the task. (a)(2) The effects of surface contact on the amplitude of vibrissa movements in one rat. The angular displacement of different vibrissae are seen to decrease when they contact a texture as opposed to sweep the air without contact. Panels (a)(1) and (a)(2) adapted from Carvell GE and Simons DJ (1990) Biometric analyses of vibrissal tactile discrimination in the rat. *Journal of Neuroscience* 10: 2638–2648; see also Carvell GE and Simons DJ (1995) Task- and subject-related differences in sensorimotor behavior during active touch. *Somatosensory & Motor Research* 12: 1–9. A similar task was pioneered by Guic-Robles (Guic-Robles E, Valdivieso C, and Guajardo G (1989) *Behavioural Brain Research* 31: 285–289) and recently extended to mice (Celikel T and Sakmann B (2007) *Proceedings of the National Academy of Sciences USA* 104: 1395–1400). (b)(1) Apparatus for a task to test distance discrimination. The width of the aperture is adjusted between two values, 'narrow' or 'wide.' Differences of 1.5 mm, that is, 62 mm versus 63.5 mm, were generally irresolvable, but differences of 3 mm were resolvable. At the start of each session, the rat is placed in the outer reward chamber with the sliding door closed. When the door is opened, the rat enters the center discrimination chamber, centers in the nose poke, and samples the aperture with its vibrissae. The rat then backs into the outer reward chamber and pokes its nose into either the left or right nose poke to receive a water reward: a left nose poke if the aperture is narrow and a right nose poke if the aperture is wide. (b)(2) Mean percentage of correct discriminations for an ensemble of rats in which vibrissae were sequentially and systematically removed. Note the decrease in performance with the total number of vibrissae removed. Panels (b)(1) and (b)(2) adapted from Krupa DJ, Matell MS, Brisben AJ, Oliveira LM, and Nicolelis MAL (2001) Behavioral properties of the trigeminal somatosensory system in rats performing whisker-dependent tactile discriminations. *Journal of Neuroscience* 21: 5752–5763; see also Shuler MG, Krupa DJ, and Nicolelis MA (2002) Integration of bilateral whisker stimuli in rats: Role of the whisker barrel cortices. *Cerebral Cortex* 12: 86–97. (c)(1) Apparatus for a task to test fine discrimination in horizontal offsets of two bilaterally spaced bars. The horizontal locations of the poles were changed between trials in steps of 0.1 mm. At the start of each session, the rat enters the center discrimination chamber, centers in the nose poke, and samples the poles with its vibrissae. The rat then backs into the outer reward chamber and pokes its nose into either the left or the right reward cell to receive a water reward; a specific offset is randomly paired with a specific side for each rat. (c)(2) Distribution of performance thresholds after discrimination training with the complete C row of vibrissae, after trimming down to one vibrissa, C2, and retraining, and for control animals with no vibrissae. (c)(1) and (c)(2) adapted from Knutsen PM, Pietr M, and Ahissar E (2006) Haptic object localization in the vibrissal system: Behavior and performance. *Journal of Neuroscience* 26: 8451–8464.

NRSC: 01351



f0015 **Figure 3** Behavior that involves the confluence of touch and position signals during exploratory whisking. (a) Cartoon that depicts a task to detect the position of an object relative to the rat's head with only one vibrissa. This task differentiates between labeled line-schemes that involve multiple vibrissae but no knowledge of vibrissa position and haptic-schemes that depend on both touch and position neural streams (dashed arrows) but do not require multiple vibrissa. (b) Details of the training and testing arena. Discrimination trials begin when an animal trips the nose poke sensor, which causes either the rostral or the caudal stimulus pin to descend into the vibrissa field. Lever presses in response to the rewarded, that is, S+, stimulus, either the rostral or caudal pin for each animal, result in a drop of water in the fluid dispenser. Lever presses in response to the unrewarded, that is, S−, stimulus have no effect. (c) Cumulative behavioral responses for one session, averaged separately over S+ and S− trials. The line and shaded regions give the mean ±2 standard error of measurement cumulative lever press counts. The gray arrows at 0.5 s mark the time after which the error regions remain nonoverlapping. Adapted from Mehta SB, Whitmer D, Figueroa R, Williams BA, and Kleinfeld D (2007) Active spatial perception in the vibrissa scanning sensorimotor system. *PLoS Biology* 5: e15.

s0045 ## Midbrain Loop

p0085 A intermediate-level loop incorporates the superior colliculus and includes connections that cross the midline (**Figure 4**). The superior colliculus is a laminar, midbrain structure in which each layer is nominally devoted to integrating sensory and motor information relevant to a particular sensory modality. In rat, the intermediate and deep layers of the colliculus appear to be devoted to general somatic sensorimotor processing, with the more

NRSC: 01351

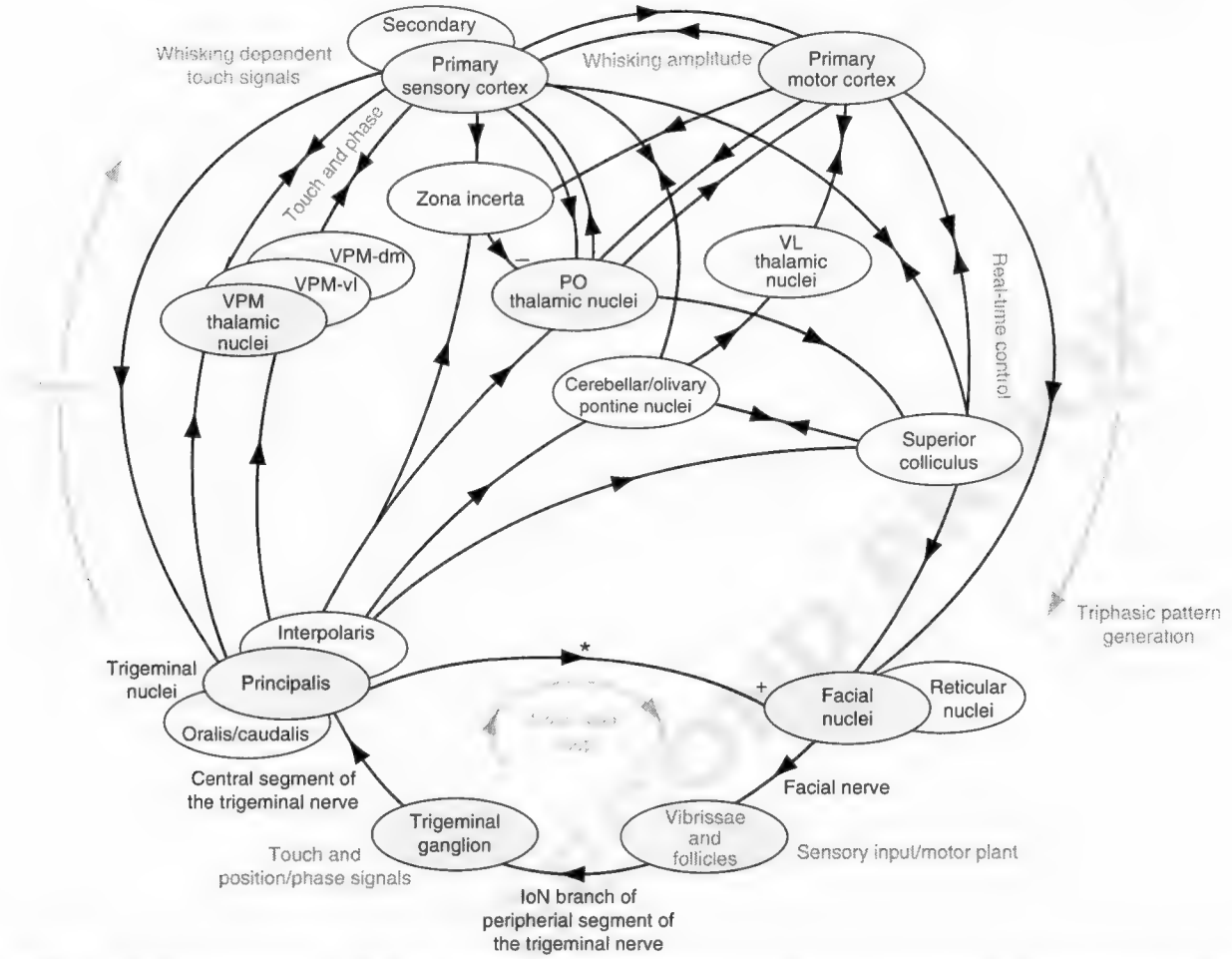


Figure 4 Cartoon of the anatomy of nested, vibrissa sensorimotor loops. The proposed connections are gleaned from the work of very many laboratories and provide a coarse roadmap of the flow of neuronal signals. Only pathways of direct relevance to active sensing with vibrissae are shown, with the most studied areas, from the perspective of electrophysiology, shown in yellow. Subdivisions of each area that are not shown in the figure may be described below. Basal ganglion pathways (Mercier BE, Legg CR, and Glickstein M (1990) *Proceedings of the National Academy of Sciences USA* 87: 4388–4392; Deniau JM, Kita H, and Kitai ST (1992) *Neuroscience Letters* 144: 202–206), are not included as they have only recently received attention in the vibrissa community (Hoffer ZS, Arantes HB, Roth RL, and Alloway KD (2005) *Journal of Comparative Neurology* 488: 2–100). Nor has the loop between neocortex and the hippocampus been considered (Buzsaki G (1996) *Cerebral Cortex* 6: 81–92; Chrobak JJ, Lorincz A, and Buzsaki G (2000) *Hippocampus* 10: 457–465), a bias that reflects current ignorance in the role of these structures in sensorimotor control. The asterisk labels the shortest sensorimotor feedback pathway, which is a single-synapse from the principal trigeminal nucleus to the lateral aspect of the facial nucleus. **Hindbrain loops: (vibrissae → trigeminal ganglion)** The vibrissae are innervated by both slowly and rapidly adapting sensory afferents (**Figure 1**) that originate from the infraorbital nerve (Dorfl J (1985) *Journal of Anatomy* 142: 173–184; Rice FL A, Mance A, and Munger BL (1986) *Journal of Comparative Neurology* 252: 154–174; Leiser SC and Moxon KA (2006) *Journal of Neurophysiology* 95: 3125–3145). **(trigeminal ganglion → trigeminal nucleus)** Sensory inputs from the trigeminal ganglion project to the principal sensory nucleus (PrV) and the spinal trigeminal nuclei oralis (SpVO), interpolaris (SpVI), and caudalis (SpVC; Torvik A (1956) *Journal of Comparative Neurology* 106: 51–132; Clarke WB and Bowsher D (1962) *Experimental Neurology* 6: 372–383). The PrV and SpVI nuclei and the magnocellular portion of SpVC have somatotopic maps of the vibrissae ('barrelettes'; Ma PM and Woolsey RA (1984) *Brain Research* 306: 374–379); SpVO receives sensory input from the vibrissae yet does not contain a map (Belford GR and Killackey HP (1979) *Journal of Comparative Neurology* 188: 63–74; Belford GR and Killackey HP (1979) *Journal of Comparative Neurology* 183: 305–322). Last, there is particularly high internuclear connectivity among the SpVC and SpVO nuclei (Jacquin MF, Chiaia NL, Haring JH, and Rhoades RW (1990) *Somatosensory & Motor Research* 7: 399–420). The PrV nucleus receives collateral excitatory input from the SpVC and SpVI nuclei and inhibition from the SpVI nucleus (Furuta T, Timofeeva E, Nakamura K, et al. (2008) Inhibitory gating of vibrissal inputs in the brainstem. *Journal of Neuroscience* 28: 1789–1797). **(trigeminal nuclei → facial nuclei)** The facial nucleus contains five subnuclei, of which the lateral subnucleus is involved in vibrissa control (Papez JW (1927) *Journal of Comparative Neurology* 42: 159–191; Martin MR and Lodge D (1977) *Brain Research* 38: 206–210). Vibrissa areas SpVC, PrV, and SpVI connect to the lateral subnucleus, primarily through ipsilateral projections. The trigeminal loop is closed by direct projection from PrV, SpVC, and SpV1 to the facial nucleus (Erzurumlu RS and Killackey HP (1979) *Journal of Comparative Neurology* 188: 75–86; Hattox AM, Priest CA, and Keller A (2002) *Journal of Comparative Neurology* 442: 266–276) and indirect pathways within the hindbrain via the pontomedullary reticular formation (Dauvergne C, Pinganaud G, Buisseret P, Buisseret-Delmas C, and Zerari-Mailly F (2001) *Neuroscience Letters* 311: 109–112;

NRSC: 01351

rostral and lateral areas responding to vibrissa-related inputs from the contralateral trigeminal nuclei. Descending afferents from the superior colliculus project to the lateral subnucleus of the contralateral facial nucleus to complete the loop. An additional input that converges to the same laminae arises from ipsilateral vibrissa primary motor (M1) cortex.

Zerari-Mailly F, Pinganaud G, Dauvergne C, Buisseret P, and Buisseret-Delmas CJ (2001) *Journal of Comparative Neurology* 429: 80–93). The direct projection, and possibly the indirect projection, is predominantly excitatory and results in positive feedback (Nguyen Q-T and Kleinfeld D (2005) *Neuron* 45: 447–457). **(facial nucleus → vibrissae)** The lateral aspect facial nucleus sends projections to the intrinsic muscles surrounding each vibrissa (Arvidsson J (1982) *Journal of Comparative Neurology* 211: 84–92; Dorfl J (1982) *Journal of Anatomy* 135: 147–154; Dorfl J (1985) *Journal of Anatomy* 142: 173–184; Arvidsson J and Rice F L (1991) *Journal of Comparative Neurology* 309: 1–16), and medial aspects are believed to project to the extrinsic muscles (**Figures 2(a)–2(c)**; Klein B and Rhoades R (1985) *Journal of Comparative Neurology* 232: 55–69; Isokawa-Akesson M and Komisaruk BR (1987) *Experimental Brain Research* 65: 385–398). The lateral subnucleus of the facial nucleus contains a somatotopic map of the vibrissae (Martin MR and Lodge D (1977) *Brain Research* 38: 206–210). **Midbrain loops: (trigeminal nuclei → superior colliculus)** The trigeminal nuclei project to vibrissa somatotopic areas of the superior colliculus (Drager UC and Hubel DH (1976) *Journal of Neurophysiology* 39: 91–101; Killackey H and Erzurumlu R (1981) *Journal of Comparative Neurology* 201: 221–242; Huerta M, Frankfurter A, and Harting J (1983) *Journal of Comparative Neurology* 220: 147–167; Steindler DA (1985) *Journal of Comparative Neurology* 237: 155–175; Bruce LL, McHaffie JG, and Stein BE (1987) *Journal of Comparative Neurology* 262: 315–330; Jacquin M, Barcia M, and Rhoades RW (1989) *Journal of Comparative Neurology* 282: 45–62; Benett-Clarke CA, Chiaia NL, Jacquin MF, and Rhoades RW (1992) *Journal of Comparative Neurology* 320: 323–338). Hemelt ME and Keller A (in press) Superior colliculus control of vibrissa movements. *Journal of Neurophysiology*. The connection from nucleus SpVI appears to be the strongest (Killackey H and Erzurumlu R (1981) *Journal of Comparative Neurology* 201: 221–242; Huerta M, Frankfurter A, and Harting J (1983) *Journal of Comparative Neurology* 220: 147–167; Jacquin M, Barcia M, and Rhoades RW (1989) *Journal of Comparative Neurology* 282: 45–62); it terminates in the intermediate and deep layers of the lateral and rostral aspects of the colliculus. The projections from the trigeminal ganglia to colliculus are likely to be collaterals of projections to thalamus (Benett-Clarke CA, Chiaia NL, Jacquin MF, and Rhoades RW (1992) *Journal of Comparative Neurology* 320: 323–338; Mantle-St. John LA and Tracey DJ (1987) *Journal of Comparative Neurology* 255: 259–271). **(superior colliculus → facial nucleus)** The intermediate and deep layers of the colliculus project to the lateral subnucleus of the facial nerve nucleus (Isokawa-Akesson M and Komisaruk BR (1987) *Experimental Brain Research* 65: 385–398; Miyashita E, Keller A, and Asanuma H (1994) *Experimental Brain Research* 99: 223–232; Miyashita E, and Shigemi M (1995) *Neuroscience Letters* 195: 69–71). **(trigeminal nuclei → cerebellum)** The trigeminal nuclei provide vibrissa sensory input to the cerebellum via a direct pathway, that is, the SpVI nucleus projects directly to the cerebellum (Woolston DC, LaLonde JR, and Gilson JM (1982) *Journal of Neurophysiology* 48: 160–173), and two indirect pathways, that is, the SpVI and SpVC nuclei project via the inferior olive climbing fibers and the PrV, SpVI, and SpVC nuclei project via pontine mossy fibers (Huerta M, Frankfurter A, and Harting J (1983) *Journal of Comparative Neurology* 220: 147–167; Steindler DA (1985) *Journal of Comparative Neurology* 237: 155–175; Jacquin M, Barcia M, and Rhoades RW (1989) *Journal of Comparative Neurology* 282: 45–62; Mantle-St. John LA and Tracey DJ (1987) *Journal of Comparative Neurology* 255: 259–271; Smith RL (1973) *Journal of Comparative Neurology* 148: 423–446; Watson CRR and Switzer III RC (1978) *Neuroscience Letters* 10: 77–82; Swenson RS, Kosinski RJ, and Castro AJ (1984) *Journal of Comparative Neurology* 222: 301–311). Projections from the trigeminal nuclei to the inferior olive overlap those from the olive to the cerebellum; the target areas in the cerebellum include *crura* I and II and the paramedian lobule and uvula (Huerta M, Frankfurter A, and Harting J (1983) *Journal of Comparative Neurology* 220: 147–167; Watson CRR and Switzer III RC (1978) *Neuroscience Letters* 10: 77–82); all these areas have facial receptive fields. **(superior colliculus ↔ cerebellum)** The colliculus sends projections to the cerebellar cortex, including target areas *crura* I and II, through both the inferior olive and the pons (Kassel J (1980) *Brain Research* 202: 291–305). The deep cerebellar nuclei send a projection back to the colliculus (Lee HS, Kosinski RJ, and Mihailoff GA (1989) *Neuroscience* 28: 725–734; Westby GW, Collinson C, and Dean P (1993) *European Journal of Neuroscience* 5: 1378–1388; Westby GW, Collinson C, Redgrave P, and Dean P (1994) *European Journal of Neuroscience* 6: 1335–1342) to form a 'colliculus → cerebellum → colliculus' loop. **Forebrain loops: (trigeminal nuclei → dorsal thalamus)** The PrV nucleus sends ascending projections to ventral posteromedial (VPM) thalamic nuclei, and the SpVI nucleus sends projections to posterior (PO) nuclei and to the ventral-lateral area of VPM (VPM-vl) thalamus as well as the dorsal-medial area of VPM (VPM-dm) thalamus (Lund RD and Webster KE (1967) *Journal of Comparative Neurology* 130: 313–328; Smith RL (1973) *Journal of Comparative Neurology* 148: 423–446; Erzurumlu RS and Killackey HP (1980) *Neuroscience*. 5: 1891–1901; Hoogland PV, Welker E, and Van der Loos H (1987) *Experimental Brain Research* 68: 73–87; Mantle-St. John LA and Tracey DJ (1987) *Journal of Comparative Neurology* 255: 259–271; Jacquin M, Barcia M, and Rhoades RW (1989) *Journal of Comparative Neurology* 282: 45–62; Killackey HP, Jacquin M, and Rhoades RW (1990) In: *Development of Sensory Systems in Mammals*, pp. 403–429. New York: Wiley; Chiaia NL, Rhoades RW, Bennett-Clark CA, Fish SE, and Killackey HP (1991) *Journal of Comparative Neurology* 314: 201–216; Benett-Clarke CA, Chiaia NL, Jacquin MF, and Rhoades RW (1992) *Journal of Comparative Neurology* 320: 323–338; Diamond ME, Armstrong-James M, Budway MJ, and Ebner FF (1992) *Journal of Comparative Neurology* 319: 66–84; Williams MN, Zahm DS, and Jacquin MF (1994) *European Journal of Neuroscience* 6: 429–453; Veinante P and Deschenes M (1999) *Journal of Neuroscience* 19: 5085–5095; Pierret T, Lavallee P, and Deschenes M (2000) *Journal of Neuroscience* 20: 7455–7462. Yu C, Derdikman D, Haidarliu S, and Ahissar E (2006) Parallel thalamic pathways for whisking and touch signals in the rat. *PLoS Biology* 4:e124; Simons DJ, Carvell GE, Kyriazi HT, and Bruno RM (2007) Thalamocortical conduction times and stimulus-evoked responses in the rat whisker-to-barrel system. *Journal of Neurophysiology* 98: 2842–2847; Masri R, Bezdudnaya T, Trageser JC, and Keller A. (in press) Encoding of stimulus frequency and sensor motion in the posterior medial thalamic nucleus. *Journal of Neurophysiology*.)The representation of the vibrissae forms a somatotopic map ('barreloids') in VPM thalamus (Van Der Loos H (1976) *Neuroscience Letters* 2: 1–6; Sugitani M, Yano J, Sugai T, and Ooyama H (1990) *Experimental Brain Research* 81: 346–351) and a diffuse map in PO thalamus (Nothias F, Peschanski M,

NRSC: 01351

s0050 **Cerebellar Loops**

p0090 The pontine–cerebellar system appears to function at a hindbrain level in a loop that involves direct connections from the contralateral SpVI nucleus and indirect connections between contralateral trigeminal nuclei and the ipsilateral superior colliculus (Figure 4). For the latter case, the trigeminal nuclei project to both the pons and the inferior olive, which in turn directly project to crura 1 and 2 in the cerebellum. Similar inputs, which project to the same crura in cerebellum,

and Besson J-M (1988) *Brain Research* 447: 169–174; Fabri M and Burton H (1991) *Brain Research* 538: 351–357) and VPM-vl (Pierret T, Lavallee P, and Deschenes M (2000) *Journal of Neuroscience* 20: 7455–7462). **(trigeminal nuclei → zona incerta)** Nuclei in zona incerta (ZI) consist exclusively of inhibitory projection neurons; those involved in vibrissa somatosensation receive input from SpVI (Kolmac CI, Power BD, and Mitrofanis J (1998) *Journal of Comparative Neurology* 396: 544–555). ZI forms a negative (-) feedback connection to PO thalamus (Trageser JC and Keller A (2004) *Journal of Neuroscience* 24: 8911–8915; Lavallee P, Urbain N, Dufresne C, Bokor H, Acsady L, and Deschenes M (2005) *Journal of Neuroscience* 25: 7489–7498) that is inactivated only by descending input from vibrissa cortex Urbain N and Deschenes M (2007) Motor cortex gates vibrissal responses in a thalamocortical projection pathway. *Neuron* 56: 714–725 **(dorsal thalamus ↔ neocortex)** Thalamic regions VPM, PO, and ZI project to primary (S1), secondary (S2), and posterior ventral areas of sensory cortex, and cortex sends feedback projections to VP, PO, and the trigeminal nuclei (Wise SP and Jones EG (1977) *Journal of Comparative Neurology* 175: 129–158; Donoghue JP, Kerman KL, and Ebner FF (1979) *Journal of Comparative Neurology* 183: 647–664; Donoghue JP and Kitai ST (1981) *Journal of Comparative Neurology* 201: 1–13; Carvell GE and Simons DJ (1987) *Journal of Comparative Neurology* 265: 409–427; Hoogland PV, Welker E, and Van der Loos H (1987) *Experimental Brain Research* 68: 73–87; Koralek K, Jensen KF, and Killackey HP (1988) *Brain Research* 463: 346–351; Welker E, Hoogland PV, and van der Loos H (1988) *Experimental Brain Research* 73: 411–435; Jacquin MF, Wiegand MR, and Renehan WE (1990) *Journal of Neurophysiology* 64: 3–27; Chiaia NL, Rhoades RW, Bennett-Clark CA, Fish SE, and Killackey HP (1991) *Journal of Comparative Neurology* 314: 201–216; Chiaia NL, Rhoades RW, Fish SE, and Killackey HP (1991) *Journal of Comparative Neurology* 314: 217–236; Diamond ME, Armstrong-James M, Budway MJ, and Ebner FF (1992) *Journal of Comparative Neurology* 319: 66–84; Deschênes M, Bourassa J, and Parent A (1996) *Neuroscience* 72: 679–687; Lévesque M, Charara A, Gagnon S, Parent A, and Deschênes M (1996) *Brain Research* 709: 311–315; Shepherd GM and Svoboda K (2005) *Journal of Neuroscience* 25: 5670–5679; Landisman CE and Connors BW (2007) VPM and PoM Nuclei of the rat somatosensory thalamus: Intrinsic neuronal properties and corticothalamic feedback. *Cerebral Cortex.* 17: 2853–2865, Urbain N and Deschenes M (2007) A new thalamic pathway of vibrissal information modulated by the motor cortex. *Journal of Neuroscience* 27: 12407–12412; Bokor H, Acsady L, and Deschenes M (2008) Vibrissal responses of thalamic cells that project to the septal columns of the barrel cortex and to the second somatosensory area. *Journal of Neuroscience* 28: 5169–5177); The projection from ZI thalamus to S1 cortex is unique in providing an inhibitory input (Chapin JK, Schneider JS, Nicolelis M, and Lin C-S (1990) *Science* 248: 1553–1556; Nicolelis MAL, Chapin JK, and Lin RCS (1992) *Brain Research* 577: 134–141). **(direct intercortical connections)** Vibrissa S1 cortex forms reciprocal projections with other vibrissa sensory areas in neocortex (Carvell GE and Simons DJ (1987) *Journal of Comparative Neurology* 265: 409–427; Chapin JK, Sadeq M, and Guise JLU (1987) *Journal of Comparative Neurology* 263: 326–346; Welker E, Hoogland PV, and van der Loos H (1988) *Experimental Brain Research* 73: 411–435; Fabri M and Burton H (1991) *Journal of Comparative Neurology* 311: 405–424; Hoffer ZS, Hoover JE, and Alloway KD (2003) *Journal of Comparative Neurology* 466: 525–544; Chakrabarti S and Alloway KD (2006) *Journal of Comparative Neurology* 498: 624–636) and with vibrissa motor (M1) cortex (White EL and deAmicis RA (1977) *Journal of Comparative Neurology* 175: 455–482; Fabri M and Burton H (1991) *Journal of Comparative Neurology* 311: 405–424; Aroniadou VA and Keller A (1993) *Journal of Neurophysiology* 70: 1493–1553; Keller A (1993) *Cerebral Cortex* 3: 430–441; Miyashita E, Keller A, and Asanuma H (1994) *Experimental Brain Research* 99: 223–232; Izraeli R and Porter LL (1995) *Experimental Brain Research* 104: 41–54; Veinante P and Deschenes M (2003) *Journal of Comparative Neurology* 464: 98–103; Hoffer ZS, Arantes HB, Roth RL, and Alloway KD (2005) *Journal of Comparative Neurology* 488: 82–100; Chakrabarti S and Alloway KD (2006) *Journal of Comparative Neurology* 498: 624–636). The representation of the vibrissae forms a somatotopic map in S1 cortex (Woolsey TA, Welker C, and Schwartz RH (1974) *Journal of Comparative Neurology* 164: 79–94; Durham D and Woolsey TA (1977) *Brain Research* 137: 169–174)-'barrels'- and S2 (Carvell GE and Simons DJ (1986) *Somatosensory Research* 3: 213–237; Kleinfeld D and Delaney KR (1996) *Journal of Comparative Neurology* 375: 89–108). Note that M1 is taken as the parasagittal agranular medial area. **(indirect intercortical connections)** Feedback from neocortex to thalamus via projections from cortical layer 6 provides a pathway for different cortical columns and regions to intact in thalamus (Deschenes M, Veinante P, and Zhang Z-W (1998) *Brain Research Reviews* 28: 286–308). This effect is enhanced by an effective intrathalamic connection mediated by thalamoreticular and recticulothalmic projections (Crabtree JW, Collingridge GL, and Isaac JT (1998) *Nature Neuroscience* 1: 289–394; Crabtree JW and Isaac JT (2002) *Journal of Neuroscience* 22: 8754–8761; Golomb D, Ahissar E, and Kleinfeld D (2005) *Journal of Neurophysiology* 95: 1735–1750). **(neocortex → superior colliculus)** Both sensory and motor cortices send descending projections to the superior colliculus (Wise SP and Jones EG (1977) *Journal of Comparative Neurology* 175: 129–158; Killackey H and Erzurumlu R (1981) *Journal of Comparative Neurology* 201: 221–242; Welker E, Hoogland PV, and van der Loos H (1988) *Experimental Brain Research* 73: 411–435; Mercier BE, Legg CR, and Glickstein M (1990) *Proceedings of the National Academy of Sciences USA*87: 4388–4392). Cellular interactions between the descending cortical M1 projection to colliculus and from the colliculus to the facial nucleus support the relay of motor commands to the facial nucleus (Miyashita E and Shigemi M (1995) *Neuroscience Letters*195: 69–71). **(motor cortex → reticular nuclei)** A direct connection from vibrissa M1 cortex to nuclei in the reticular formation (Miyashita E, Keller A, and Asanuma H (1994) *Experimental Brain Research* 99: 223–232; Hattox AM, Priest CA, and Keller A (2002) *Journal of Comparative Neurology* 442: 266–276) is suggestive of a central pattern generator (CPG) by analogy with the CPG for mastication (Nozaki S, Iriki A, and Nakamura Y (1986) *Journal of Neurophysiology* 55: 806–825) and provides descending control of the vibrissae. The ambiguus and parvocellular reticular nuclei in the medulla, as well as the pontine reticular nucleus, are capable of evoking vibrissa movement and further receive input from M1 cortex (Hattox AM, Priest CA, and Keller A (2002) *Journal of Comparative Neurology* 442: 266–276). Critically, direct input from M1 terminates in the lateral facial nucleus and may directly drive the vibrissae (Grinevich V, Brecht M, and Osten P (2005) *Journal of Neuroscience* 25: 8250–8258).

NRSC: 01351

t0010 **Table 2** Afferent nuclei to the lateral aspect of the facial nucleus

Afferent nucleus	*VMCtx afferent*	*Evoked movement*	*Transmitter*
Myelencephalon (medulla)			
Dorsal motor nucleus of the vagus	x		
Reticular nucleus of the medulla	x		
Intermediate reticular nucleus	x		GABA, Gly
Lateral reticular nucleus	x		
Ambiguus nucleus	x	x	
Gigantocellular reticular nucleus	x		GABA, Gly, 5-HT
Parvocellular reticular nucleus	x	x	
Spinal vestibular nuclei	x		GABA, Gly
External cuneate nucleus			
Nucleus solitary tract			
Raphe magnus, pallidus, obscurus			5-HT
Paragigantocellular reticular nucleus			
Spinal trigeminal nucleus			GABA, Gly
Hypoglossal nucleus			
Metencephalon (pons)			
Pontine reticular nucleus	x	x	GABA, Gly
Ventral parabrachial nucleus	x		
Kölliker-Fuse nucleus	x		
Paralemniscal nucleus	x		GABA, Gly
Lateral parabrachial nucleus	x		
Subpedencular tegmental nucleus	x		
Intertrigeminal nucleus	x		
Subcoeruleus nucleus	x		
Ventral nucleus of the lateral lemniscus			
Motor trigeminal nucleus			
Pediculopontine tegmental			
Medial parabrachial nucleus			
Mesencephalon (midbrain)			
Deep mesencephalic nucleus	x		
Oculomotor nucleus	x		
Central gray	x		
Superior colliculus	x	x	
Red nucleus	x	x	
Edinger-Westphal nucleus	x		
Pararubral nucleus	x		
Nucleus raphe dorsalis			
Interstitial nucleus of medial longitudinal fasciculus			
Retrorubral nucleus			
Nucleus Darkschewitsch			
Substantia nigra			
Primary motor cortex (VMCtx)	–	x	Glutamate

The listings are based on anatomical studies. Neurons in the lateral facial nucleus integrate inputs from about 40 presynaptic sources (Fay RA and Norgren R (1997) *Brain Research Reviews* 25: 276–290). These include reticular motor nuclei that are potentially involved with the generation of the oscillatory drive for rhythmic whisking, such as the parvocellular nucleus (Mogoseanu D, Smith AD, and Bolam JP (1994) *Experimental Brain Research* 101: 427–438; Hattox AM, Priest CA, and Keller A (2002) *Journal of Comparative Neurology* 442: 266–276), reticular nuclei that are involved with other oromotor behaviors (Travers JB (1995) In: Paxinos G (ed.) *The Rat Nervous System*, 2nd edn., pp. 239–255. San Diego: Academic Press), such as suckling and licking, trigeminal sensory nuclei, whose input to the facial nucleus completes a feedback loop that encompasses the vibrissae; cerebellar deep nuclei, whose input also completes a feedback loop (Huerta M, Frankfurter A, and Harting J (1983) *Journal of Comparative Neurology* 220: 147–167), input from the superior colliculus (Miyashita E, Keller A, and Asanuma H (1994) *Experimental Brain Research* 99: 223–232; Miyashita E and Shigemi M (1995) *Neuroscience Letters* 195: 69–71), and direct input from the primary motor cortex (Grinevich V, Brecht M, and Osten P (2005) *Journal of Neuroscience* 25: 8250–8258). The column labeled 'VMCtx afferent' denotes that the nucleus receives a projection from primary motor cortex. VMCtx, vibrissa primary motor cortex. The column labeled 'Evoked movement' indicates that activation of this region in anesthetized animals leads to vibrissa movement.

arise from the intermediate and deep layers of the superior colliculus. The relative means by which these inputs contribute to a pronounced sensory response in crus 2, and a more restricted response in crus 1, is unknown. Finally, the cerebellar Purkinje cells form synapses on the cerebellar nuclei, which provide output projections to superior colliculus to complete this intermediary-level loop.

NRSC: 01351

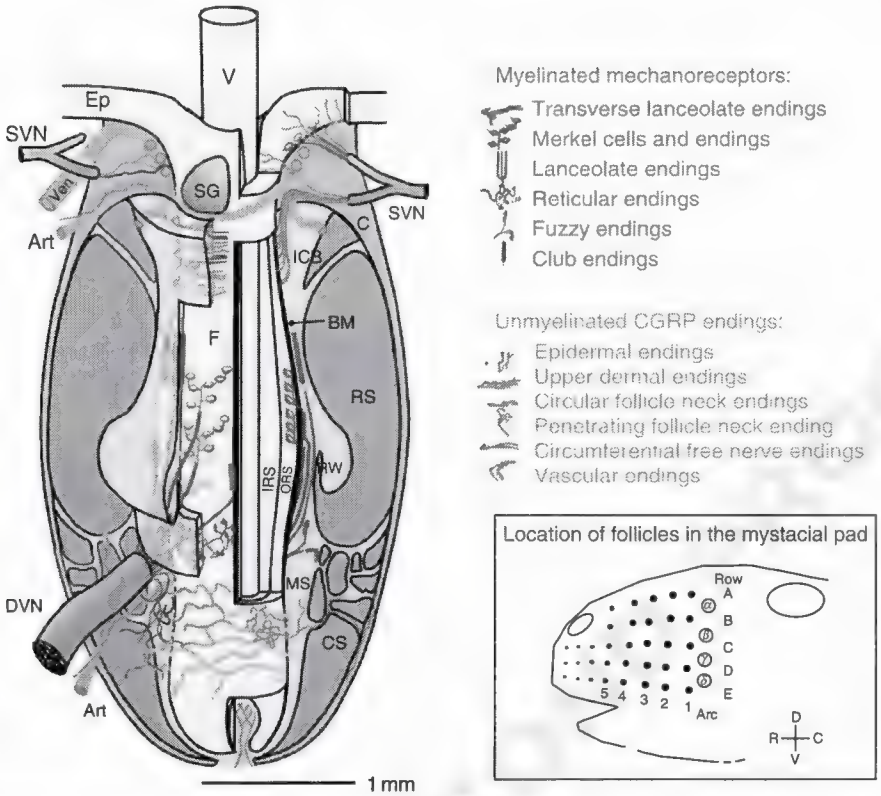


Figure 5 The follicle contains both superficial (SVN) and deep (DVN) nerve terminals that report both self-movement and contact of the vibrissa. The follicle sits in the mystacial pad as part of an array of five rows and roughly ten arcs of follicle/vibrissa units (**insert in lower right corner**). Rows are labeled by letters and arcs by numbers. The four posterior vibrissa, referred to as straddlers, are labeled by Greek letters. In the awake and aroused animal, the sinuses (CS and RS) are engorged with blood, which stiffens the structure. Both self-movement and touch are presumed to be coded by both the superficial and deep nerves, which project to the trigeminal ganglion and have similar passive response properties (Waite PME and Jacquin MF (1992) *Journal of Comparative Neurology* 322: 233–245). The DVN ultimately projects to the PrV, SpVO, SpVI, and SpVC trigeminal nuclei (Hayashi H (1985) *Journal of Comparative Neurology* 237: 195–215; Jacquin MF, Stennett RA, Renehan WE, and Rhoades RW (1988) *Journal of Comparative Neurology* 267: 107–130), and the SVN has been reported to project only to SpVC (Martin Deschenes, unpublished observations). This illustration was adapted from Arvidsson J and Rice FL (1991) Central projections of primary sensory neurons innervating different parts of the vibrissae follicles and intervibrissal skin on the mystacial pad of the rat. *Journal of Comparative Neurology* 309: 1–16; see also Rice FL, Fundin BT, Pfaller K, and Arvidsson J (1994) *Experimental Brain Research* 99: 233–246. A mechanical model of the follicle is given by Mitchinson B, Gurney KN, Redgrave P, et al. (2004) *Proceedings of the Royal Society of London, Series B: Containing Papers of a Biological Character* 271: 2509–2516. V, vibrissa; SG, sebacceous gland; RW, ringwulst; RS, ring sinus; ORS, outer root sheath; MS, mesenchymal sheath; IRS, inner root sheath; ICB, inner conical body; F, follicle; Ep, epidermis; CS, cavernous sinus; C, follicle-sinus-complex capsule; BM, basement membrane; CGRP, calcitonin gene-related peptide; and Art, arteriole.

s0055 **Thalamic-Forebrain Loop**

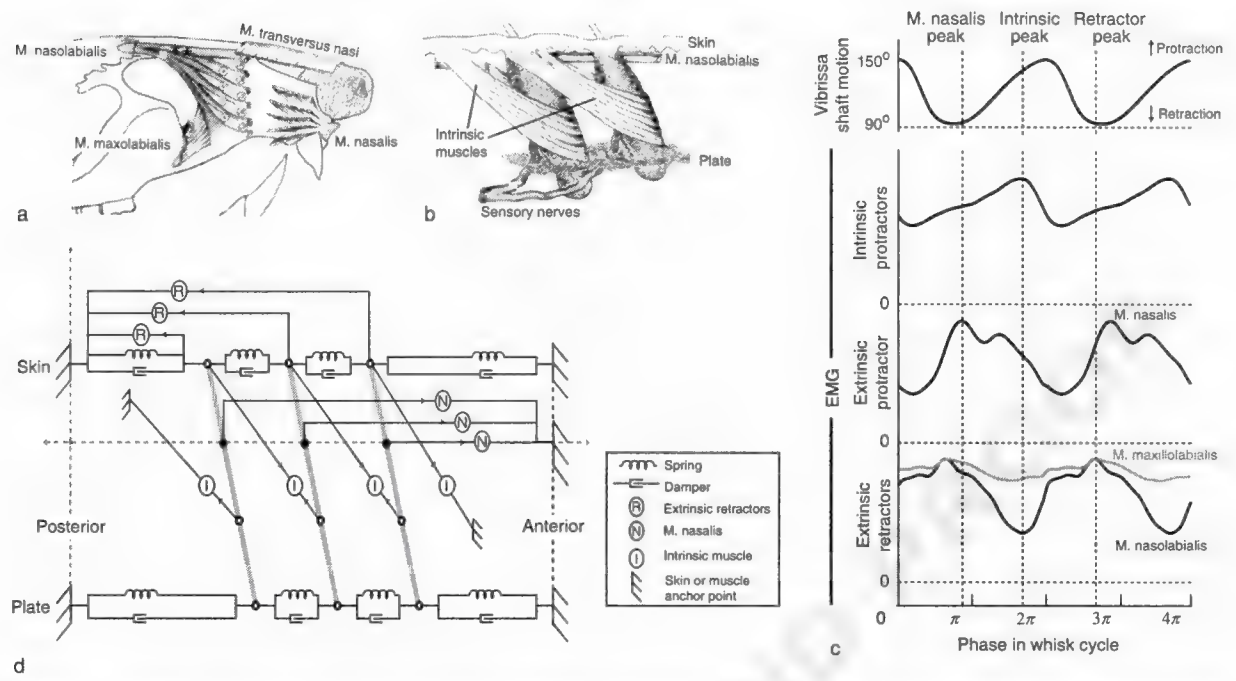
p0095 Multiple structures in ventral and dorsal thalamus receive input from the trigeminal nuclei. Only one of these, zona incerta (ZI) in the ventral thalamus, projects directly back to the superior colliculus (**Figure 4**), where it forms inhibitory connections with the superior colliculus. Thus, ZI thalamus appears to function as a forebrain-level intermediary in a loop that involves the trigeminal nuclei and the colliculus. Further, inhibitory projections from ZI thalamus serve to gate afferents from PO thalamus to vibrissa SI cortex. This gate is removed by descending inputs from vibrissa M1 cortex.

Neocortical Loop s0060

p0100 Cortex receives input from the trigeminal nuclei along four streams that pass through the thalamus (**Figure 4**):

1. The well-known lemniscal pathway that ascends from the PrV nucleus via the central region of the ventral posterior medial (VPM) thalamus and projects to vibrissa primary somatosensory (S1) cortex. Neurons in VPM thalamus rapidly respond to stimulation of a single vibrissa in anesthetized animals, whose receptive fields are referred to as barreloids. Similarly, neurons in the granular layer

NRSC: 01351



f0030 **Figure 6** Geometry, musculature, and motion of the follicles and vibrissae. (a) Drawing of extrinsic musculature in mouse; a similar pattern occurs in rat. Four extrinsic muscles invade the mystacial pad while maintaining external attachment points. The retractor M. nasolabialis attaches dorsal–caudal to the pad and runs superficially below the skin. A second retractor, m. maxillolabialis, attaches ventral–caudal to the pad and fuses with the fibers of m. nasolabialis as they invade the pad. M. nasalis attaches rostral to the pad at the nasal septum and runs deep to the follicles as it extends caudally. M. transversus nasi lies transverse to the snout and runs superficially through the pad. (b) Drawing of intrinsic musculature in mouse. The intrinsic muscles join adjacent follicles (insert in **Figure 5**) of a single row. Each muscle attaches medially and laterally to the superior part of the caudal follicle while forming a sling around the lower third of the rostral follicle. The skin and other connective tissue, such as the fibrous plate, provide a passive restoring force. Superficial extrinsic muscles run just below the skin. (c) A mechanical model of a row of three vibrissae, shown in the rest state, to illustrate how the extrinsic and intrinsic muscles pull on the vibrissae. The attachment points are illustrated for the springs, dampers, and muscles, which together from an active vasoelastic element. The approximate relationship between these points is conserved, but the figure is not drawn to scale. Arrows indicate the direction of muscle forces, which point away from the attachment points. (d) Average vibrissa motion and muscle activity from a head-restrained rat. Each whisk was linearly mapped from time onto the range of 0 to 2π radians and the average taken across phase. Average traces (1750 whisks) are repeated to display two cycles; only motion along the A–P axis is shown. The rectified electromyogram values were normalized by the maximum voltage of each trace. The dashed vertical lines indicate the three phases of average muscle activity. The drawings in panels (a) and (b) were adapted from Dorfl J (1982) The musculature of the mystacial vibrissae of the white mouse. *Journal of Anatomy* 135: 147–154; see also Dorfl J (1985) The innervation of the mystacial region of the white mouse: A topographical study. *Journal of Anatomy* 142: 173–184, and the model and data in panels (c) and (d) from Hill DN, Bermejo R, Zeigler HP, and Kleinfeld D (2008) Biomechanics of the vibrissa motor plant in rat: Rhythmic whisking consists of triphasic neuromuscular activity. *Journal of Neuroscience* 28: 3438–3455.

of S1 cortex respond to stimulation of a single vibrissa, whose receptive fields are formed by afferents from VPM thalamus and are referred to as barrels.

2. The well-known paralemniscal pathway that ascends from the rostral part of the SpVI nucleus, passes through posterior medial (PO) thalamus, and projects down to the superior colliculus as well as up to agranular layers 1 and 5 in S1 cortex, vibrissa secondary somatosensory (S2), and vibrissa motor (M1) cortices. Neurons in PO thalamus receive inhibitory projections from ZI thalamus; this inhibitory block is relieved by projections from M1 cortex to PO thalamus.

3. A recently described extralemniscal pathway that ascends from the caudal part of the SpVI nucleus, passes through the ventrolateral border of VPM (VPM-vl) thalamus, and projects to S1 and S2 cortices. Neurons in VPM-vl thalamus rapidly respond to stimulation of multiple vibrissae in anesthetized animals.

4. A recently described extralemniscal pathway that ascends from the part of the PrV nucleus that contains large neurons with multivibrissa responses, passes through the dorsomedial border of VPM (VPM-dm) thalamus that lies next to PO thalamus, and projects to S1 cortex. Neurons in VPM-dm thalamus rapidly respond to stimulation of multiple vibrissae in anesthetized animals.

NRSC: 01351

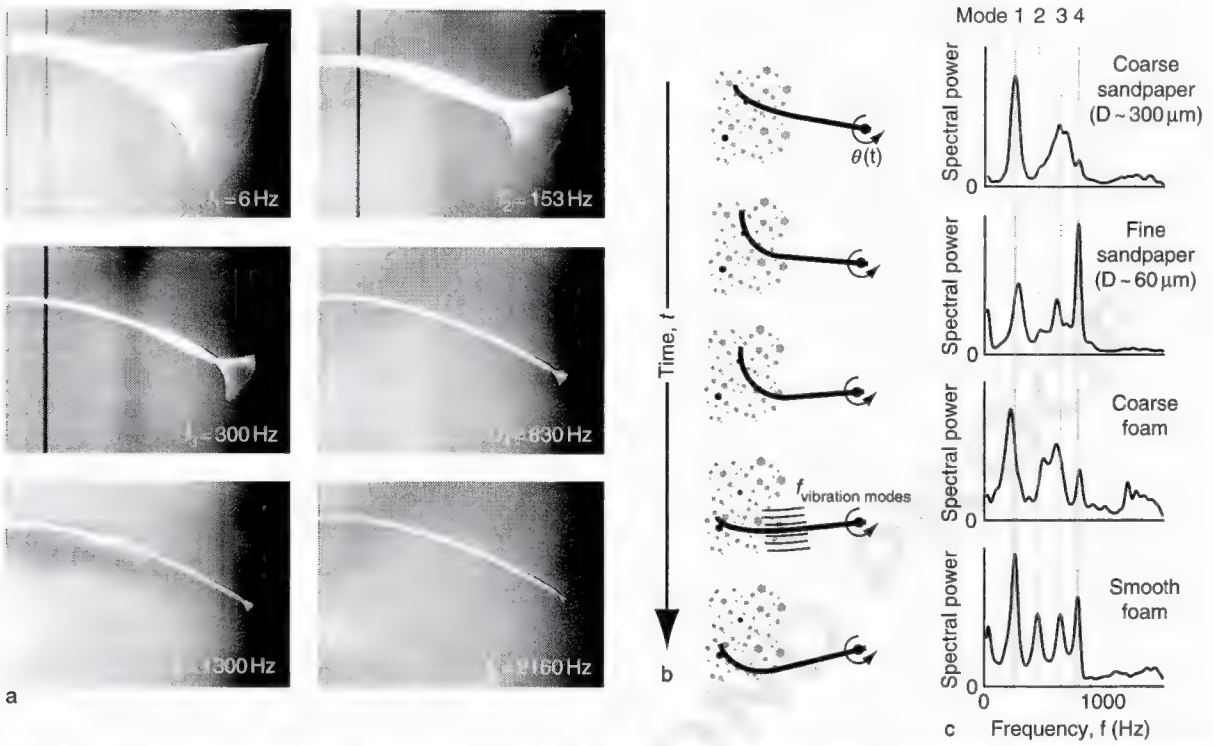


FIG0004 **Figure 7** Dynamics of a single vibrissa. (a) Photographs of the motion of the straddler vibrissa γ (see insert, **Figure 5**) at successive resonant frequencies. The vibrissa was glued to a small voice coil that was driven by a wave generator. Note that the displacements are shifted to the finer and more distal parts of the vibrissa at progressively higher-order modes. Data was taken in the laboratory following reports by Hartmann (Hartmann MJ, Johnson NJ, Towal RB, and Assad C (2003) Mechanical characteristics of rat vibrissae: Resonant frequencies and damping in isolated whiskers and in the awake behaving animal. *Journal of Neuroscience* 23: 6510–6519) and Moore (Neimark MA, Andermann ML, Hopfield JJ, and Moore CI (2003) Vibrissa resonance as a transduction mechanism for tactile encoding. *Journal of Neuroscience* 23: 6499–6509; Ritt JT, Andermann ML, and Moore CI (2008) Emdodied information processing: vibrissa mechanics and texture features shape micromotions in actively sensing rats. *Neuron* 57: 599–613). (b) Cartoon that shows how the drag on a vibrissa can couple to the intrinsic mechanical vibrations (modes) of the vibrissa via 'stick–slip' friction. This effect may be relevant for the encoding of texture. Adapted from Mehta SB and Kleinfeld D (2004) Frisking the whiskers: Patterned sensory input in the rat vibrissa system. *Neuron* 41: 181–184. (c) Spectral power of the vibrations measured at the base of a vibrissa artificially whisked across different textures, in support of a model in which different surfaces preferentially excite different modes of a vibrissa (Moore CI and Andermann ML (2005) In: Ebner FF (ed.) *Neural Plasticity in Adult Somatic Sensory-Motor Systems*. Boca Raton, FL: CRC Press). Adapted from Fend M, Bovet S, Yokoi H, and Pfeifer R (2003) An active artificial whisker array for texture discrimination. In: *Proceedings of the IEEE/RSJ International Conference on Intelligent Robots and Systems* (IROS), Las Vegas, NV, October.

All four thalamic areas receive feedback projections from the infragranular layers of S1 and S2 cortices. Further, VPM-dm thalamus receives feedback projections from M1 cortex.

p0105 There is evidence for the segregation of neuronal signals among the different pathways. The lemniscal pathway appears to convey a combination of touch and position signals while the extralemniscal pathway appears to convey primarily touch-based signals. The evidence for signaling along the paralemniscal pathway is inconsistent. Activation of neurons in PO thalamus in anesthetized animals occurs via feedback from S1 cortex. On the other hand, during whisking neurons in PO thalamus may be driven directly by sensory input and report vibrissa position. Independent of this segregation of information, the thalamic nuclei interact via reciprocal connections to the reticular thalamic nucleus, which may lead to a mixing of touch and position signals, among others. Further, sensory and motor cortex interact through corticocortical projections, and there is considerable feedback among thalamic-mediated connections between cortical areas (**Figure 4**). This implies that sensory and motor functions are likely to be distributed throughout these areas.

The cortical loop is closed by corticospinal-like p0110 projections from M1 cortex to the vibrissa areas of the facial nucleus, as well as by projections from both S1 and M1 cortices to the superior colliculus, which in turn sends descending projections to motor neurons in the facial nucleus. By analogy with the

NRSC: 01351

anatomy of corticospinal projections in primates, there may be undiscovered projections from vibrissa S1 cortex to the facial nucleus.

s0065 **Back to the Brain Stem**

p0115 Two more points bear on the nested topology of the vibrissa system. The first is that a single synaptic connection from neurons in the trigeminal complex to those in the facial nucleus (* in **Figure 4**) is paralleled, from hindbrain to midbrain to forebrain, by connections of increasing complexity. The second and related issue is that the motor neurons in the lateral facial nucleus appear as arbitrators of activity from loops at all levels, receiving input from neurons in nearly 40 identified nuclei (**Table 2**). This makes the motor neurons arbitrators of motor commands to the vibrissae.

s0070 Mechanics of the Vibrissae

p0120 The vibrissae are shaped as round, tapered beams. Videographs of the vibrissae as rats whisk clearly show that the vibrissae flex as a consequence of the muscular forces that propel them forward at their base as well as the forces that act on contact (**Figure 1(b)**). A result of this flexibility is that, as for all extended mechanical systems, individual vibrissae exhibit a set of resonances (**Figure 7(a)**). The lowest-order resonance exhibits bending all along the vibrissae, while higher-order resonances exhibit bending that is localized toward the tip.

p0125 What are the potential ethological roles that vibrations of the vibrissae can play? One is that a vibrissa can twang when it contacts an object, so that touch will yield a rapid succession of taps rather than a single tap. The frequency of these taps will depend on the location of contact along the shaft of the vibrissa but will be in the order of the roughly 100 Hz resonant frequencies. This rate is sufficient to induce short-term synaptic plasticity; so mechanical resonance may contribute to the transmission probability of a contact event.

p0130 The vibrations of the vibrissae may also play a role in sensing texture. The vibrissae may alternately stick and slip as they are dragged across a rough surface (**Figure 7(b)**). As the vibrissa slips, the resultant vibrations of the shaft will be a superposition of the intrinsic vibrations of the vibrissa. It is natural to posit that differences between surfaces are expressed by the extent to which different modes are favored. In particular, when the tip of a vibrissa is moved across surfaces of differing roughness, the set of frequencies of the vibration is essentially the same for all surfaces, but the relative amplitude associated with each vibration will depend on the detailed properties of the surface (**Figure 7(c)**).

Transmission of High-Frequency Signals s0075

p0135 The timing of neuronal signals from the initial contact of a vibrissa with an object to their representation in vibrissa S1 cortex is central to perception. This timing is heavily dependent on the state of the animal, that is, sessile versus aroused, as mediated through synaptic changes and cellular adaptation. While modulation of the timing might complicate the processing of sensory signals, simplicities appear in two limits as signals ascend the lemniscal pathway (**Figure 4**). For punctate signals, as might occur with a sharp initial contact, there is a high probability that the signal will successfully propagate up through cortex. In contrast, for steady-state periodic signals, the probability of transmission can be low (**Figure 8**). At the level of primary sensory neurons, periodic signals are faithfully transduced up to frequencies of ~1200 Hz. However, this signal begins to degrade at the level of the PrV nucleus in brain stem, such that for vibration frequencies above ~350 Hz, roughly half the spikes are dropped (* in bottom row, second column, of **Figure 8**). By the level of VPM thalamus, roughly half the spikes are dropped for frequencies above ~35 Hz, and by the level of S1 cortex, roughly half the spikes are dropped for frequencies above ~5 Hz. Thus the ability of individual neurons to faithfully follow rapid movements of the vibrissa degrades with higher-order structures in the sensorimotor system.

p0140 How are high-frequency events, such as vibrations, encoded in cortex? First, even the response in the primary sensory cells may be insufficient to track the finest surface detail. In particular, the maximum response frequency of 1200 Hz corresponds to the rhythmic motion of the tip of a vibrissa across a corrugated surface with a pitch of only ~200 μm, which is rather coarse. Second, while neurons in S1 cortex cannot track the phase of periodic inputs above ~35 Hz, at least in anesthetized animals the high-frequency sensory inputs are coded as an approximate Poisson process (right column in **Figure 8**). It is interesting that the rate of this spike process is proportional to the logarithm of the vibration frequency of the vibrissa, that is,

$$\text{Firing Rate} \propto 2 \ln \{\text{Vibration Frequency}\} + \text{Constant}.$$

p0145 This is in the form of Weber's Law, but for frequencies rather than intensity. The coarseness of logarithmic coding suggests that comparisons of rhythmic inputs with slightly different frequencies will be problematic.

NRSC: 01351

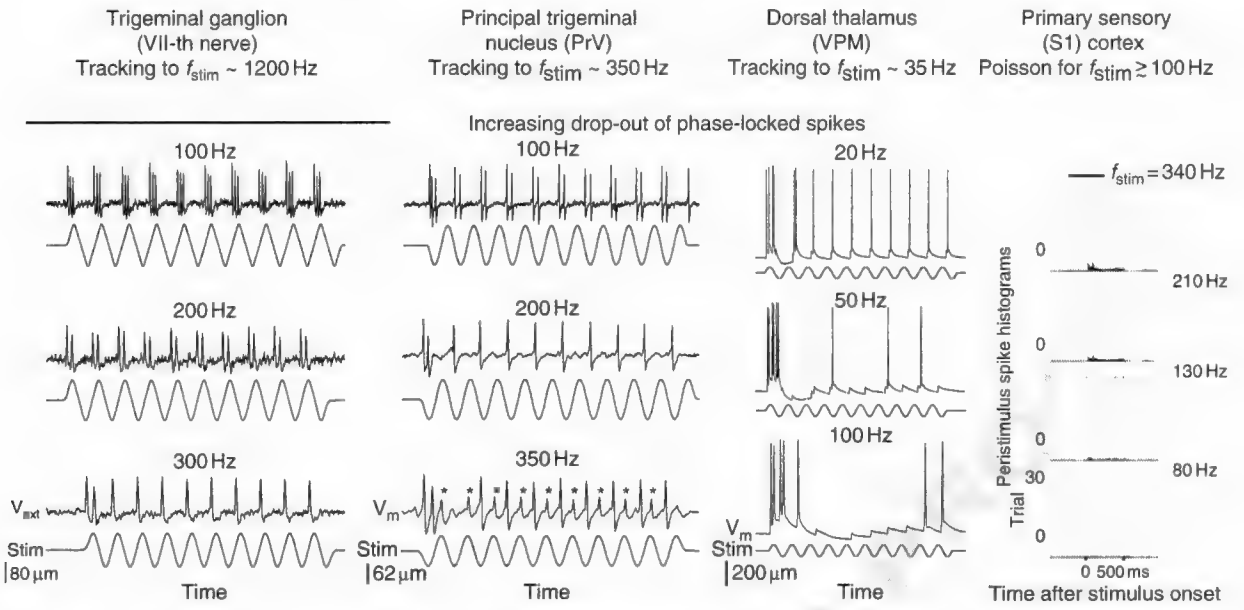


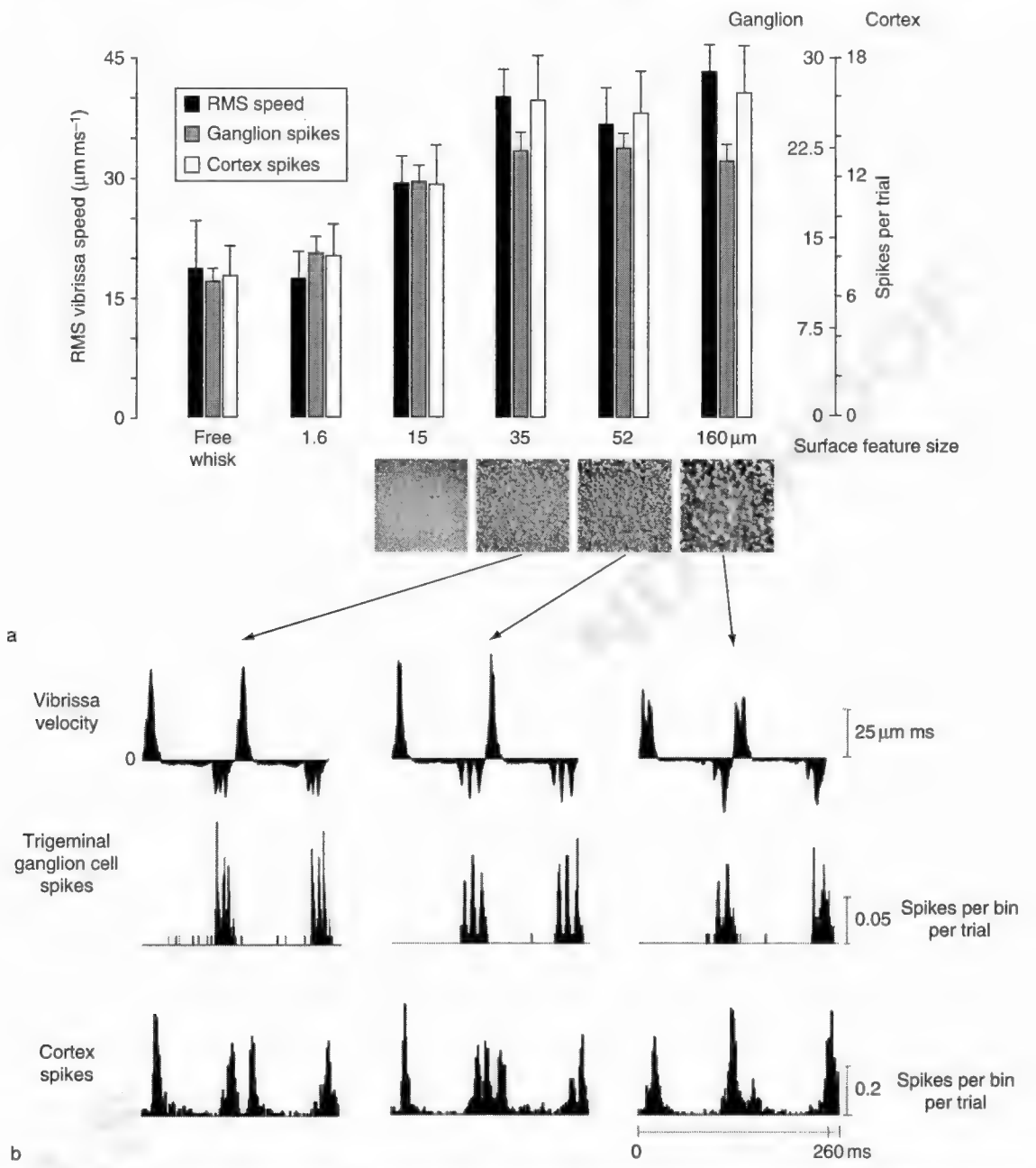
fig0040 **Figure 8** Loss in phase-locked spiking with ascending activation of vibrissa brain centers as the frequency of periodic stimulation is increased. In all cases a sinusoidal stimulus was applied to a single vibrissa in an anesthetized animal. The extracellular, single-unit responses are shown in the first and fourth columns, and intracellular responses are shown in the second and third columns. Individual units in the trigeminal ganglia respond reliably up to 1200 Hz stimulation of the vibrissa (Gottschaldt KM and Vahle-Hinz C (1981) *Science* 214: 143–186), and essentially all units respond reliably to 300 Hz. By the anatomical level of the ventral posterior medial nucleus of dorsal thalamus (VPM), the responses are phase locked to the stimulus but rather infrequent; that is, most spikes are dropped. By the level of the PrV, the responses are still phase locked to the stimulus but drop-outs (*) are significant by 350 Hz. At the level of cortex, the drop-out rate is apparently so high that phase-locked spiking is not apparent at high frequencies, yet for stimulation frequencies near 100 Hz and above, the neurons appear to fire in a largely asynchronous manner, that is, as an inhomogeneous Poisson process. Note that, at all levels, the onset of stimulation always leads to transient activation. Data in the first three columns from Deschenes M, Timofeeva E, and Lavallee P (2003) The relay of high-frequency sensory signals in the whisker-to-barreloid pathway. *Journal of Neuroscience* 23: 6778–6787, and data in the final column from Arabzadeh E, Petersen RS, and Diamond ME (2003) Encoding of whisker vibration by rat barrel cortex neurons: Implications for texture discrimination. *Journal of Neuroscience* 27: 9146–9154. The responses are different in aroused animals or anesthetized animals with activation of their cholinergic system; the responses in VPM thalamus (Castro-Alamancos MA (2002) Different temporal processing of sensory inputs in the rat thalamus during quiescent and information processing states in vivo. *Journal of Physiology* 539: 567–578.) extend to higher frequencies before attenuation, while the frequency dependence of the response in vibrissa S1 cortex is largely unchanged (Castro-Alamancos MA (2004) Absence of rapid sensory adaptation in neocortex during information processing states. *Neuron* 41: 455–464) and may further exhibit bursts of spikes (de Kock C and Sakmann B (in press) High frequency action potential bursts (100 Hz) in L2/3 and L5B thick tufted neurons in anaesthetized and awake rat primary somatosensory cortex. *Journal of Physiology*; Ewert TA, Vahle-Hinz C, and Engel AK (2008) High-frequency whisker vibration is encoded by phase-locked responses of neurons in the rat's barrel cortex. *Journal of Neuroscience* 14: 5359–5368).

s0080 ## Sensory Representation of Texture

p0150 Studies on the coding of texture typically make use of irregular surfaces of differing roughness, such as sandpapers, as stimuli. In one paradigm, artificial whisking with anesthetized animals is used to ensure a repeatable pattern of motion of individual vibrissae, whose detailed positions can be recorded with high-speed videography (**Figure 9**). Artificial whisking makes use of electrical stimulation of the facial nerve, with trains of pulses to induce rhythmic sweeps. Yet artificial whisking provides a practical means to study the variation in vibrissa movement across surfaces for the same muscular drive. Further, once the motion is recorded, one can use the stored waveforms to control piezoelectric manipulators that move the vibrissa in a repeatable manner. The caveats of this approach are twofold: first, the resultant motion is abnormal in that the three phases of natural motor activity (**Figure 6(c)**) are reduced to one and, second, sensation may be altered in that extrinsic movement of the vibrissae approximates self-induced movement.

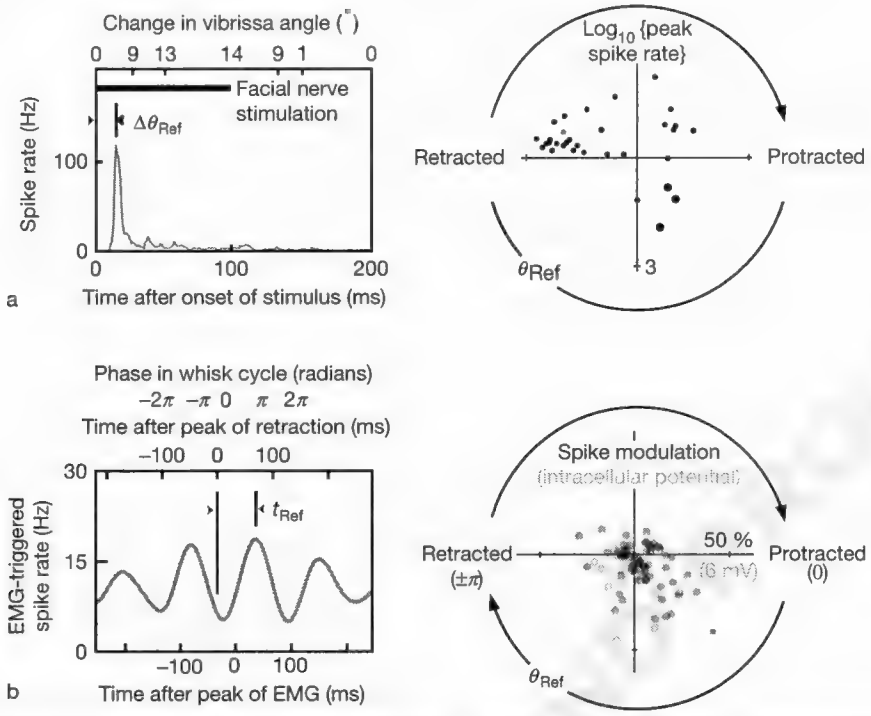
p0155 The motion of the vibrissae across different sandpapers in the artificial whisking paradigm has been characterized in two ways. First, variations in motion were quantified in terms of the root-mean-square (RMS) speed of the shaft of individual vibrissae. The RMS speed initially increased in a progression from smooth to rough surfaces, then reached an asymptote as the size of the surface features reached ~35 μm (**Figure 9(a)**). Concomitant with this asymptote in

NRSC: 01351



f0045 **Figure 9** Evidence that vibrissa motions induced by textured surfaces are encoded by both average spike rate and temporal variations in the rate. (a) Texture coding by the average rate of neuronal firing. The spike rate is plotted for texture-induced vibrations, quantified by the root-mean-square (RMS) speed of the horizontal vibrissa motion, averaged across 100 trials of 500 ms each. The average spike count per trial was pooled from ten trigeminal ganglion neurons and 12 neurons in vibrissa S1 cortex (granular layer); note the different scales for spike counts. The insets show the surfaces. (b) Texture coding by patterns in the firing rate for three examples. The top line shows variations in velocity of a vibrissa as it moves across one of three different textures. The second line shows the peristimulus time histograms, with 0.2-ms bins, for a unit in the trigeminal ganglion. The final line shows the peristimulus time histograms for a unit in S1 cortex. Each profile is the average of 100 trials. Data adapted from Arabzadeh E, Zorzin E, and Diamond ME (2005) Neuronal encoding of texture in the whisker sensory pathway. *PLoS Biology* 3(e17): 155–165; the discrimination of different textures is discussed by von Helmendahl M, Itskov PM, Arabzadeh E, and Diamond ME (2007) Neuronal activity in rat barrel cortex underlying texture discrimination. *PLoS Biology* 5: e305.

NRSC: 01351



f0050 **Figure 10** Encoding of vibrissa position in the hindbrain and forebrain. (a) Spiking output from primary sensory neurons of the trigeminal ganglion was recorded during vibrissa motion induced by 5 Hz electrical stimulation of the facial motor nerve. The left panel shows the trial-averaged response of the reference signal for one neuron; the angle $\Delta\theta_{Ref}$ is the extent of protraction, relative to the initial retracted position, at the peak of the neuronal response. The right panel summarizes the data for all cells. From Szwed M, Bagdasarian K, and Ahissar E (2003) Encoding of vibrissal active touch. *Neuron* 40: 621–630. The radial coordinate is the logarithm of the peak spike rate, and the angular coordinate is the phase within the whisk cycle. (b) Responses in vibrissa S1 cortex measured as animals whisked without contact. The data on the left show an example of the correlation between spiking and the peak of the electromyogram (EMG). The scale on top accounts for the lag between vibrissa position and the EMG (Berg RW and Kleinfeld D (2003) *Journal of Neurophysiology* 89: 104–117); the time t_{Ref} is the peak of cortical spiking relative to the fully retracted position. The panel on the right summarizes the data for all cells from these extracellular measurements, for which the radial coordinate is the modulation of the spike–EMG correlation, as well as cells from recent intracellular studies, for which the radial coordinate is the maximum intracellular depolarization. The bias in spiking as a function of phase in the whisk cycle comes slightly earlier than that for the membrane depolarization, as expected for a threshold process. Data from Fee MS, Mitra PP, and Kleinfeld D (1997) Central versus peripheral determinants of patterned spike activity in rat vibrissa cortex during whisking. *Journal of Neurophysiology* 78: 1144–1149; Mehta SB and Kleinfeld D (2004) Frisking the whiskers: Patterned sensory input in the rat vibrissa system. *Neuron* 41: 181–184; and Crochet S and Petersen CCH (2006) Correlating whisker behavior with membrane potential in barrel cortex of awake mice. *Nature Neuroscience* 9: 608–609.

speed, the spike rate of units in both the trigeminal ganglion and vibrissa S1 cortex also achieved an asymptotic value. This implies that average measures cannot distinguish among different coarse surfaces. In contrast, a second analysis considered the full time dependence of the velocity for motion across surfaces of different roughness. This measure exhibited clear changes as surface features doubled and tripled in size (**Figure 9(b)**). Further, neurons in the trigeminal ganglion faithfully tracked these changes, with directional preference, consistent with their ability to track high-frequency vibrations (**Figure 8**). At the level of S1 cortex, there were repeatable differences in the spike rate for all sandpapers, although many details of the timing were not tracked (**Figure 9(b)**).

p0160 The data suggest that the motion of a vibrissa across a textured surface is dominated by stick–slip events (**Figure 7(b)**), this conclusion has been partially verified with awake animals in natural textural settings. Further, while primary sensory cells can encode different textures, the algorithm for encoding a natural ensemble of textures in terms of cortical spike rates remains an open issue, as does the issue of the fidelity of that encoding.

Sensory Representation of Object Location

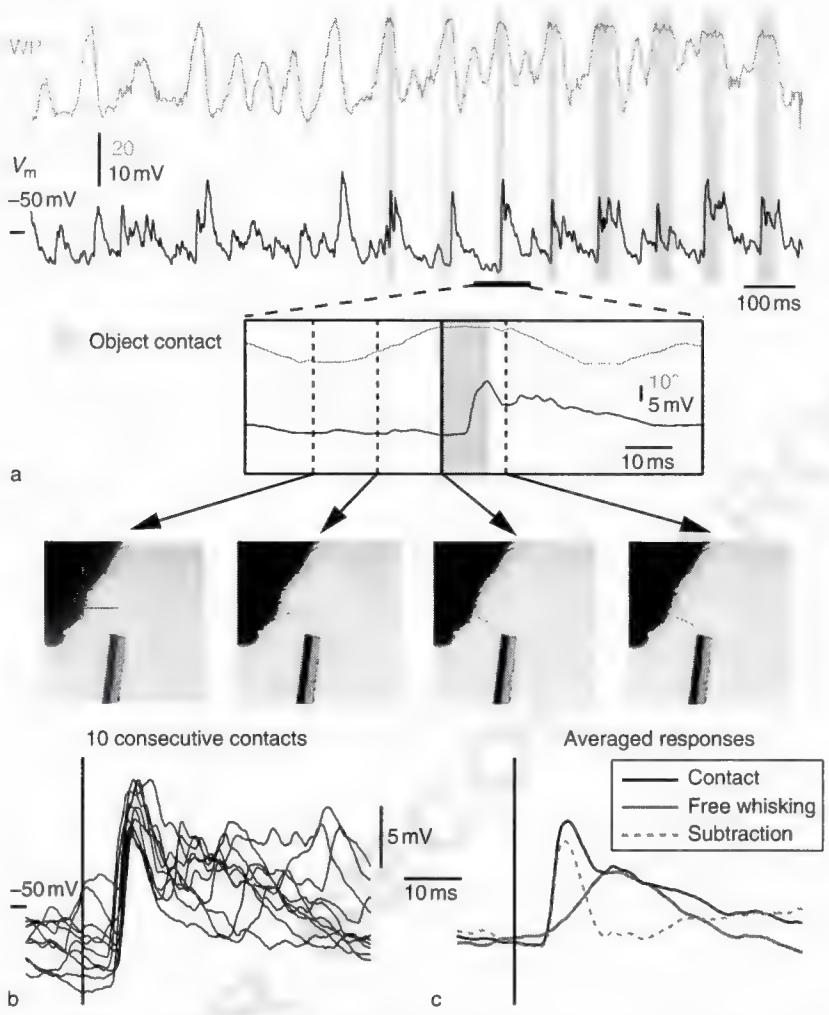
s0085

Neuronal Signals of Vibrissa Position

s0090

p0165 There is a lack of evidence for spindle fibers, the transduction mechanism for proprioception, in the facial musculature, as well as a lack of evidence for descending inputs to primary sensory neurons.

NRSC: 01351



f0055 **Figure 11** Intracellular potential of neurons in primary vibrissa cortex of a head-fixed mouse during active touch. (a) The mouse whisked in air both without contact (left sides of top two traces) and with contact against an object (right sides) when it thrust its vibrissae forward. The intracellular potential is marked by V_m (black), the videographed vibrissa position is marked by WP (green), and contact is marked by a gray bar. Note that the rest level of the cell is relatively depolarized. The box corresponds to an expansion of one contact event, with videographs of the contact event shown below. (b) The superposition of ten consecutive contacts shows the reliability and temporal precision of the intracellular response. (c) Intracellular responses evoked by contact with an object were averaged (blue) and compared with the average response aligned with respect to the peak of the vibrissa position for whisking in air (WP in (a)). The response evoked by contact was faster and larger than that evoked by free whisking; dashed red line marks the subtraction of the two responses. Adapted from Crochet S and Petersen CCH (2006) Correlating whisker behavior with membrane potential in barrel cortex of awake mice. *Nature Neuroscience* 9: 608–609.

Nonetheless, the results of experiments with the artificial whisking paradigm report the presence of reference signals for vibrissa position in a subset of primary sensory neurons (left panel in **Figure 10(a)**). Different neurons preferentially spiked at different angles during the whisk cycle (right panel in **Figure 10(a)**), with a bias toward protraction from the retracted position. These data, together with nerve block experiments, imply that the position signal originates from peripheral reafference.

p0170 At the level of vibrissa S1 cortex, experiments with awake animals trained to whisk in air show that the spike rates of individual cortical neurons are locked to the rhythmic motion of the vibrissae, as inferred from the electromyogram (EMG) of the intrinsic muscles (left panel of **Figure 10(b)**). This constitutes a reference signal of vibrissa position. The distribution of preferred angles extends over the entire whisk cycle, with a bias toward retraction from the protracted position. Further, intracellular measurements with head-fixed awake animals find a similar distribution of preferred angles for the peak of the excitatory postsynaptic potential. The bias in spiking as a function of phase in the whisk cycle comes earlier than that

NRSC: 01351

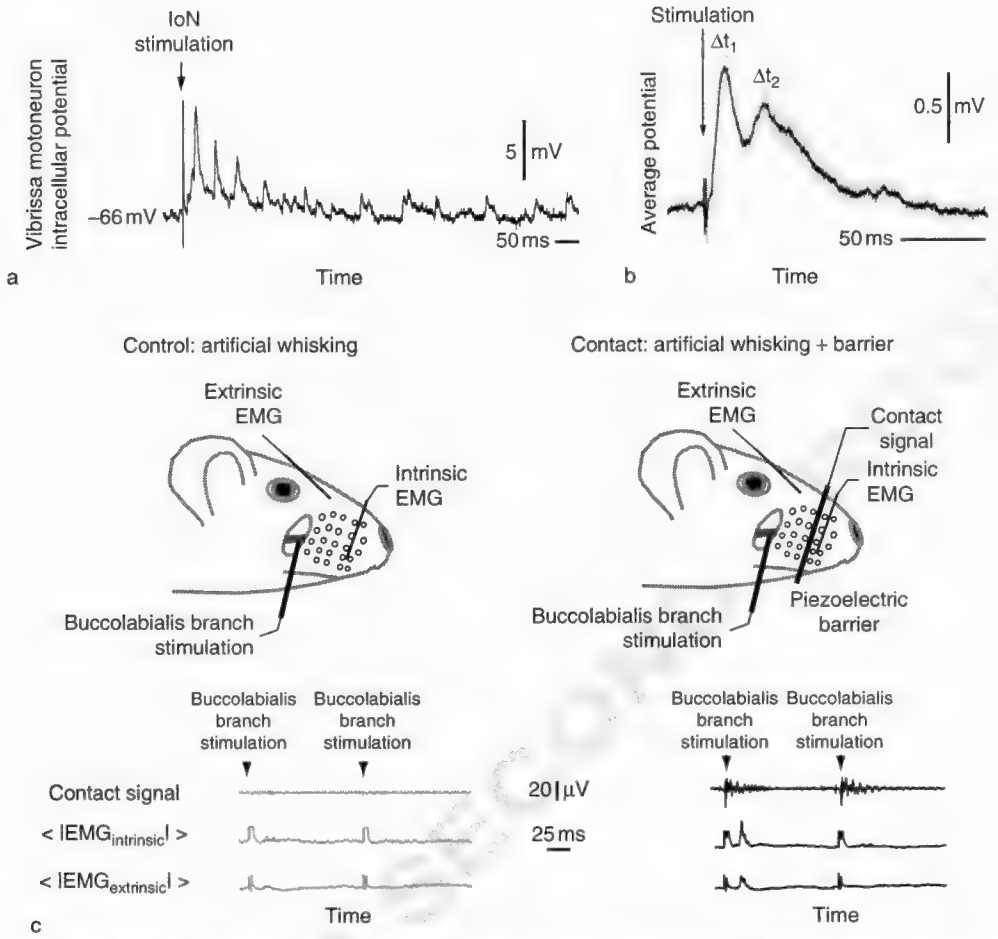


Figure 12 Sensorimotor feedback in the hindbrain (brain stem) loop. This closed loop is formed by the vibrissae follicle → trigeminal ganglion → trigeminal nuclei → facial nuclei → follicle musculature pathway; trigeminal nucleus principalis and spinal nucleus interpolaris are likely to mediate the trigeminal pathway (**Figure 6**). (a) Data from a brain stem slice preparation of juvenile animals (postnatal days 10–15) that preserves the connectivity, except that excitation of sensory terminals is replaced by shock to the infraorbital nerve (IoN), which excites vibrissa neurons in the trigeminal ganglion, and muscle output is replaced by intracellular recording from facial motor neurons in the lateral aspect of the facial nucleus. Shown are excitatory postsynaptic potentials in a motor neuron following suprathreshold stimulation (average of 20 responses) of the IoN in a slice. (b) Trial and preparation averaged intracellular response to nerve stimulation. The responses from ten trials each of 25 motor neurons were averaged together; mean, black trace; standard error of measurement, gray band. (c) The electromyogram (EMG) responses elicited by vibrissa contact in a ketamine xylazine-anesthetized adult rat. The cartoon in the top row shows the experimental setup for the contact experiment during artificial whisking (**Figure 9(a)**), for which the facial motor nerve (buccolabialis branch, driving the retractors m. nasolabialis and m. maxillolabialis; **Figure 6(a)**) is stimulated at 8 Hz with 9-mA, 50-s pulses to make the vibrissae protract. Shown are the contact signals (top traces, with control trials on the left and contact trials on the right) and consecutive averaged rectified EMG responses recorded simultaneously in intrinsic (middle traces) and extrinsic (bottom traces) vibrissa muscles. Note that the contact-induced EMG signals adapt after a single contact. Each trace is the average of 30 sweeps. Data from Nguyen Q-T and Kleinfeld D (2005) Positive feedback in a brainstem tactile sensorimotor loop. *Neuron* 45: 447–457.

for the membrane depolarization, as expected for a threshold process. Collectively, these data imply that rats ascertain the position of their vibrissa at the time of contact.

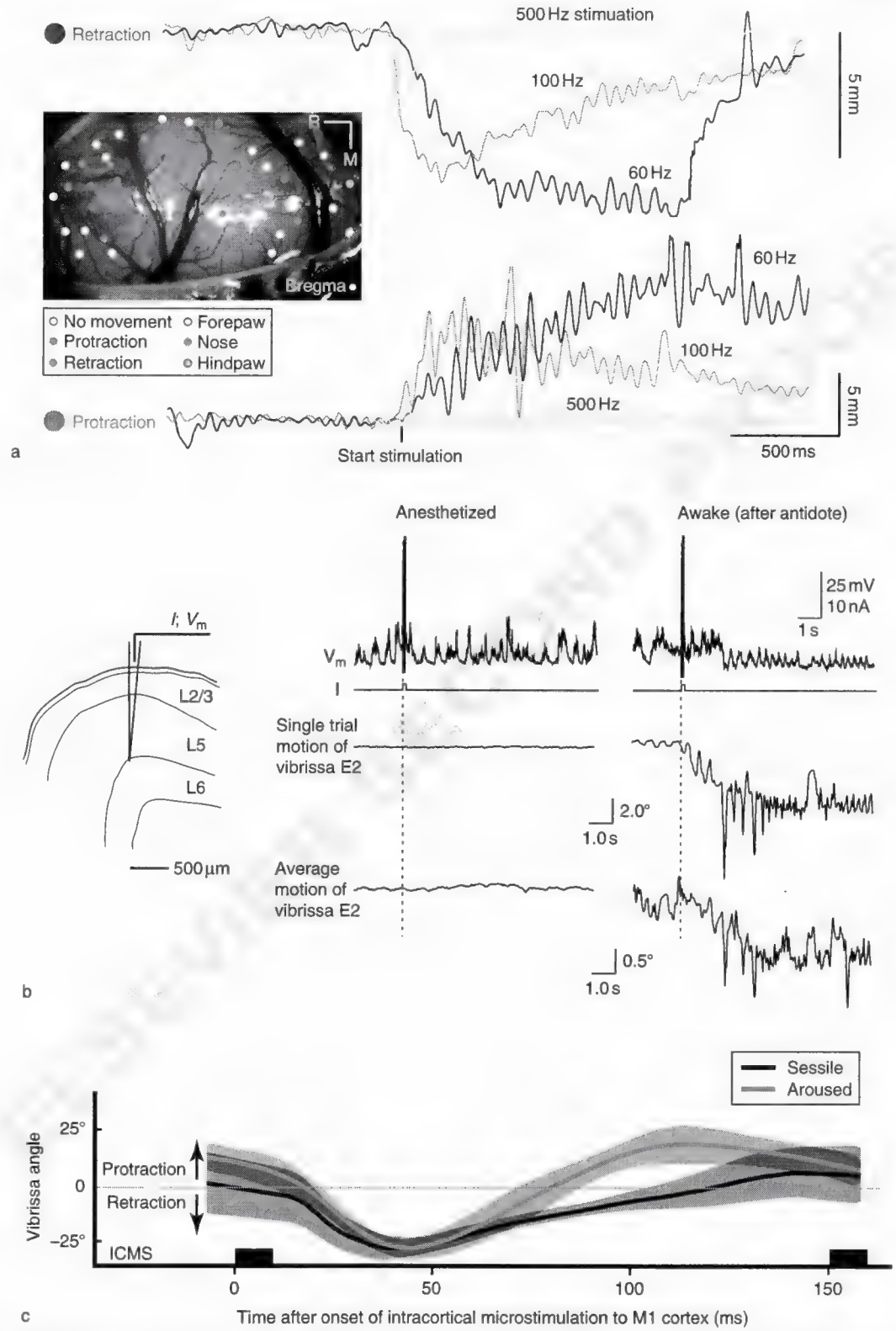
p0175 Finally, the fidelity of the reference signal in cortex depends on reward. Whisking in air that is coupled to a food reward is a factor of 2 to 3 times more coherent with vibrissa position than whisking in air that is unrewarded. This shows that reward, which is likely to heighten the attentional state of the animal, can strongly bias the nature of its sensorimotor processing.

Whisking-Dependent Contact Signals

s0095

p0180 A reliable and robust response to contact is observed at the level of the trigeminal ganglion in awake animals. The spike rate of primary sensory cells increases with increasing impact, or velocity, of contact until a

NRSC: 01351



R0065 **Figure 13** Real-time control of vibrissa position by primary motor cortex. (a) Intracortical microstimulation (ICMS) of vibrissa M1 cortex leads to retraction at a majority of stimulation sites (blue dots and associated traces at top; magnification of 3 by 5 mm image) but protraction in a medial region of frontal cortex (red dots and associated traces at bottom of image). The amplitude of the response as a function of the frequency of the microstimulation was greater for low-versus high-frequency stimulation (cf. 60 vs. 500 Hz). Data from

NRSC: 01351

saturation level is reached for angular speeds on the order of $500°s^{-1}$. There is also evidence that the radial distance to the contact point is encoded independent of the velocity.

p0185 Experiments with anesthetized animals indicate that there are robust spike responses to the initial deflection of a vibrissa along the entire ascending lemniscal pathway. Yet a systematic study of spiking at all levels in the sensorimotor hierarchy in awake animals remains to be completed, including the essential issue of spiking induced by animal-initiated contact. Nonetheless, preliminary observations of the nature of the subthreshold input to neurons in the upper layers of vibrissa S1 cortex have revealed the coexistence of whisking-related changes in subthreshold potential and changes in potential that are locked to contact (**Figure 11**). Contact signals that are referenced to vibrissa position could, in principle, be computed from the observed signals.

s0100 Sensory Modulation of Vibrissa Motion

p0190 The observation of changes in whisking on contact of the vibrissa with a wall (**Figure 1(a)**), along with changes in whisking amplitudes for whisking in air versus against a target (**Figure 2(a)**), provides evidence for changes in whisking strategy based on the task. How can this occur?

s0105 Brain Stem Mechanisms

p0195 Recent work shows that the brain stem loop exerts a transient positive feedback (**Figure 12**). At the level of *in vitro* physiology, sensory feedback from the trigeminal input to the motor neurons was measured in a brain stem slice preparation that preserves the vibrissa sensorimotor feedback pathway; see brain stem loop in **Figure 4**. Stimulation of the IoN leads solely to excitatory postsynaptic potentials in the motor neurons of the facial nucleus (**Figure 12(a)**). The latency of the response has two components, a fast Δt_1 component that presumably reflects disynaptic (IoN → trigeminal nuclei → facial nucleus) input and a slower Δt_2 component that is involved in trisynaptic or higher-order feedback in brain stem (**Figure 12(b)**). The critical issues are that feedback is both positive and rapid, that is, Δt_1 ~10 ms compared with the ~100 ms timescale of whisking.

p0200 At the level of *in vivo* physiology, the brain stem can be functionally isolated through the use of anesthesia. The artificial whisking paradigm is then used to drive the vibrissa muscles at physiological whisking rates. As a means to study sensorimotor feedback, a rigid contact detector is introduced in the trajectory of the vibrissae during alternate measurements to ascertain whether EMG responses could be elicited by contact of the vibrissae with the detector (**Figure 12(c)**). Consistent with positive feedback, contact led to a transient increase in the amplitude of the rectified EMG for both intrinsic and extrinsic muscles. This effect rapidly adapted for stimulation frequencies above 5 Hz. These data show that positive, transient feedback can lead to an increase in motor force.

p0205 Behavioral data to support transient positive sensorimotor feedback come from measurements of changes in whisking force coincident with contact. When animals whisked symmetrically yet made contact with a sensor on only one side of the face, the amplitude of the mystacial EMG on the contact side was transiently increased by 25%. These data show that the vibrissa feedback loops act to transiently increase the interval and force of contact.

s0110 Cortical Mechanisms

p0210 We conjecture that changes in whisking strategies, as opposed to transient changes in force, are regulated at the thalamocortical level. Three classes of experiments support this view. As a means to delineate the sensory representation of rhythmic input in M1 cortex, the first experimental effort made use of awake, head-fixed animals that were trained not to whisk. The observed response captured only the fundamental frequency of the input pattern for pulsatile stimuli delivered at frequencies that ranged from 5 to 20 Hz, that is, the range of exploratory whisking. This nonlinear transformation resembles the synthesis of a sinusoidal feedback signal for servocontrol of a motor.

p0215 A second class of experiments showed that vibrissa M1 cortex supports oscillations in extracellular current flow that are phase locked to whisking. These

Haiss F and Schwarz C (2005) Spatial segregation of different modes of movement control in the whisker representation of rat primary motor cortex. *Journal of Neuroscience* 25: 1579–1587. (b) Intracellular stimulation of a single neuron in M1 cortex with current I has little effect on the membrane potential V_m as well as on the motion of the vibrissae in the anesthetized state but leads to protraction of vibrissa E2 in the awake animal. Data from Brecht M, Schneider M, Sakmann B, and Margrie T (2004) Whisker movements evoked by stimulation of single pyramidal cells in rat motor cortex. *Nature* 427: 704–710. (c) Videographic data of vibrissa position in sessile versus aroused animals in response to ICMS of motor cortex. Note that ICMS in the sessile case led to retraction of the muscles, whereas stimulation in the aroused case led to a whisk cycle with retraction followed by a protraction phase. Data from Berg RW and Kleinfeld D (2003) Rhythmic whisking by rat: Retraction as well as protraction of the vibrissae is under active muscular control. *Journal of Neurophysiology* 89: 104–117. Early studies also considered the direction of motion induced by ICMS to M1 cortex (Sanderson KJ, Welker Wand Shambes GM (1984) *Brain Research* 292: 251–260; Gioanni Y and Lamarche M (1985) *Brain Research* 344: 49–61).

NRSC: 01351

signals are preserved after lesions of the IoN to block sensory input. Further, ablation of M1 cortex leads to alteration of the whisking patterns. Thus, motor cortex generates rhythmic signals that can drive normal exploratory whisking.

p0220 A final class of experiments, highlighted in Figure 13, explored the motion of the vibrissa in response to activation of vibrissa M1 cortex in both anesthetized and behaving animals. From a functional perspective, there are two contiguous motor areas. For the largest region (blue dots in Figure 13(a)), activation of tissue with a brief train of extracellular current pulses, or even depolarization of a single cell, leads to retraction of the vibrissae. For a smaller region near the midline (red dots in Figure 13(a)), activation with a brief train of extracellular current pulses leads to protraction. It is interesting that stimulation of neurons in this region with a continuous train of high-frequency pulses, rather than a brief train, can induce rhythmic whisking.

p0225 The ability of M1 motor cortex to drive whisking is enhanced when rats are awake as opposed to anesthetized. Further, this enhancement is profoundly increased in the attentive, as opposed to sessile, awake state. First, stimulation of even a single projection neuron in vibrissa M1 cortex can lead to movement of one or more vibrissae. In the awake animals, this movement is dramatically increased (Figure 13(b)). Second, while stimulation of the major fraction of vibrissa M1 cortex leads to retraction when animals are anesthetized or awake but sessile, this motion is transformed into a full whisk, with protraction and retraction, when animals are in the awake and aroused state (Figure 13(c)). This effect is mimicked by cholinergic activation of cortex, a key component of attention. Collectively, these data show that M1 cortex, in principle, can subsume full control of vibrissa movement.

s0115 Epilog

p0230 The vibrissa system in rodents has a multitude of features that make it ideal for the study of sensorimotor control in a mammal. It preserves the basic architectonics of nested feedback loops (Figure 4), yet the lissencephalic cortex of rodents makes all structures of the brain very accessible. Critical for studies of active sensation, work to date has refined a number of behavioral paradigms that tax the active nature of this sensorimotor system and define strategies for processing the sense of vibrissa-based touch (Figures 2 and 3).

p0235 Electrophysiology studies with awake, behaving animals have begun to elucidate the algorithms involved in active sensing. For texture discrimination, this is likely to include the detailed timing of spikes in vibrissa S1 cortex (Figure 9). For touch in face-centered coordinates (Figure 3), this is likely to involve the merge of touch and reference signals of vibrissa position (Figures 10 and 11). Experimental progress is anticipated to be critical to a proper understanding of active sensing in two broad, open issues.

How Do Rats Map the Space about Their Vibrissa? s0120

The main issue is whether rats maintain an abstract representation of objects that is independent of which vibrissa makes contact with an object. Or is this representation based solely on a single vibrissa (which would suggest little interaction between columnar representations)? A number of immediate issues within the realm of representation are ripe for study: p0240

- There is evidence that rats encode texture by the time between stick–slip events. How is this used to form a perception? By analogy with flutter coding in somatosensory experiments in monkeys, do rats count the number of events in a period? Or are individual periods stored? Beyond this lies the issue of whether stick–slip events are encoded across different vibrissae.
- There is evidence that primary sensory neurons can encode the radial distance of contact. How is radial distance separated from impact on contact?
- The notion of object location depends on the presence of a neuronal response that encodes contact conditioned on vibrissa position in the whisk cycle. At what level of the sensorimotor pathways do such responses first occur?
- There is evidence that the phase of the vibrissae within a whisk cycle, rather than the absolute position, is encoded. How is this accomplished? One hypothesis is that it relies on adaptation at the level of the primary sensory neurons.
- Adaptation of the neuronal response at all levels of sensory processing, and particularly at the level of thalamocortical synapses, is strong. Thus steady state responses are much different from transient responses. How does this play into the representation of sensory signals?

How Do Rats Change Their Motor Output in Response to Vibrissa-Based Touch? s0125

The main issue is how touch leads to changes in body position, whisking dynamics, and locomotion. p0245

- Rhythmic whisking can occur in the absence of sensory feedback and in the absence of high-level control. Where are the pattern generators for rhythmic whisking? Further, what form of circuitry allows these generators to stabilize at a different, single frequency from bout to bout?

NRSC: 01351

- The superior colliculus is capable of driving patterned, stereotyped motor behaviors. What is the role of the colliculus in transforming vibrissa sensory inputs into motor commands?
- Motor neurons can potentially receive feedback from sensory pathways at all levels of the brain. How are these inputs arbitrated?

See also: Barrel cortex circuits (00167); Sensorimotor Integration: Attention and the Premotor theory (01108); Sensorimotor Integration: Barrels, vibrissae and topographic representations (01109); Sensorimotor integration: models (01426).

Further Reading

Ahissar E and Zacksenhouse M (2001) Temporal and spatial coding in the rat vibrissal system. *Progress in Brain Research* 130: 75–87.

Alloway KD (2008) Information processing streams in rodent barrel cortex: The differential functions of barrel and septal circuits. *Cerebral Cortex* 18: 979–989.

Armstrong-James M (1995) The nature and plasticity of sensory processing within adult rat barrel cortex. In: Jones EG and Diamond IT (eds.) *Cerebral Cortex, Volume 11, The Barrel Cortex of Rodents*, pp. 333–374. New York: Plenum Press.

Brecht M, Grinevich V, Jin TE, Margrie T, and Osten P (2006) Cellular mechanisms of motor control in the vibrissal system. *Plflugers Archive* 453: 269–281.

Castro-Alamancos MA (2004) Dynamics of sensory thalamocortical synaptic networks during information processing states. *Progress in Neurobiology* 74: 213–247.

Deschenes M, Timofeeva E, Lavallée P, and Dufresne E (2005) The vibrissal system as a model of thalamic operations. *Progress in Brain Research* 149: 31–40.

Deschenes M, Veinante P, and Zhang Z-W (1998) The organization of cortico-thalamic pathways: Reciprocity versus parity. *Brain Research Review* 28: 286–308.

Diamond ME (1995) Somatosensory thalamus of the rat. In: Jones EG and Diamond IT (eds.) *Cerebral Cortex, Volume 11, The Barrel Cortex of Rodents*, pp. 189–220. New York: Plenum Press.

Diamond ME, von Heimendahl M, Knutsen PM, Klenfeld D and Ahissar E (in press) "Where" and "what" in the whisker sensorimotor system. *Nature Reviews of Neuroscience*.

Ebner FF and Armstrong-James MA (1990) Intracortical processes regulating the integration of sensory information. *Progress in Brain Research* 11: 129–141.

Henderson TA and Jacquin MF (1995) What makes subcortical barrels? Requite trigeminal circuitry and developmental mechanisms. In: Jones EG and Diamond IT (eds.) *Cerebral Cortex, Volume 11, The Barrel Cortex of Rodents*, pp. 123–188. New York: Plenum Press.

Hermer-Vazquez L, Hermer-Vazquez R, and Chapin JK (2005) Role of plasticity in sensorimotor transformations. In: Ebner FF (ed.) *Neural Plasticity in Adult Somatic Sensory-Motor Systems*, pp. 139–154. Boca Raton, FL: CRC Press.

Keller A (1995) Synaptic organization of the barrel cortex. In: Jones EG and Diamond IT (eds.) *Cerebral Cortex, Volume 11, The Barrel Cortex of Rodents*, pp. 221–262. New York: Plenum Press.

Kleinfeld D, Berg RW, and O'Connor SM (1999) Anatomical loops and their electrical dynamics in relation to whisking by rat. *Somatosensory and Motor Research* 16: 69–88.

Kleinfeld D, Ahissar E, and Diamond ME (2006) Active sensation: Insights from the rodent vibrissa sensorimotor system. *Current Opinions in Neurobiology* 16: 435–444.

Moore CI and Andermann ML (2005) The vibrissa resonance hypothesis. In: Ebner FF (ed.) *Neural Plasticity in Adult Somatic Sensory-Motor Systems*, pp. 21–60. Boca Raton, FL: CRC Press.

Nelson ME and MacIver MA (2006) Sensory acquisition in active sensing systems. *Comparative of Physiology A: Sensory Neural and Behavioral Physiology* 192: 573–586.

Rice FI (1995) Comparative aspects of barrel structure and development. In: Jones EG and Diamond IT (eds.) *Cerebral Cortex, Volume 11, The Barrel Cortex of Rodents*, pp. 1–76. New York: Plenum Press.

Simons DJ (1995) Neuronal integration in the somatosensory whisker/barrel cortex. In: Jones EG and Diamond IT (eds.) *Cerebral Cortex, Volume 11, The Barrel Cortex of Rodents*, pp. 263–298. New York: Plenum Press.

Travers JB (1995) Oromotor nuclei. In: Paxinos G (ed.) *The Rat Nervous System*, 2nd edn., pp. 239–255. San Diego, CA: Academic Press.

Woolsey TA (1997) Barrels, vibrissae and topographic representations. In: Adelman G and Smith B (eds.) *Encyclopedia of Neuroscience*, pp. 195–199. Amsterdam: Elsevier Press.

Wrobel A, Kublik E, and Musial P (1998) Gating of the sensory activity within barrel cortex of the awake rat. *Experimental Brain Research* 123: 117–123.

NRSC: 01351

Non-Print Items

Abstract:

Rats sweep their vibrissae through space to locate objects in their immediate environment. In essence, their view of the proximal world is generated through pliable hairs that tap and palpate objects. The texture and shape of those objects must be discerned for the rat to assess their value. Further, the location of those objects must be specified with reference to the position of the rat's head for the rat to plan its future movements. This article reviews the nature of the sensors and motor plant that govern whisking, along with the neuronal circuitry and signaling that underlie vibrissae-based sensation and sensorimotor control.

Keywords: Barrels; Barreloids; Extrinsic muscles; Foveal whisking; Infraorbital nerve; Intrinsic muscles; Phase locking; Rat; Triangulation; Vibrissae

Author and Co-author Contact Information:

D Kleinfeld
Department of Physics
University of California at San Diego
9500 Gilman Drive
La Jolla
CA 92093-0352
USA
+1 858-822-0342
+1 858-534-7696
dk@physics.ucsd.edu

Full text provided by www.sciencedirect.com
SCIENCE DIRECT®

ELSEVIER

Active sensation: insights from the rodent vibrissa sensorimotor system

David Kleinfeld[1], Ehud Ahissar[2] and Mathew E Diamond[3]

Rats sweep their vibrissae through space to locate objects in their immediate environment. In essence, their view of the proximal world is generated through pliable hairs that tap and palpate objects. The texture and shape of those objects must be discerned for the rat to assess the value of the object. Furthermore, the location of those objects must be specified with reference to the position of the rat's head for the rat to plan its movements. Recent *in vivo* and *in vitro* electrophysiological measurements provide insight into the algorithms and mechanisms that underlie these behavioral-based computations.

Addresses
[1] Department of Physics, University of California at San Diego, 9500 Gilman Drive 0374, La Jolla, California 92093, USA
[2] Department of Neurobiology, The Weizmann Institute of Science, Rehovot 76100, Israel
[3] Cognitive Neuroscience Sector, International School for Advanced Studies, via Beirut 2/4, Trieste 34014, Italy

Corresponding author: Kleinfeld, David (dk@physics.ucsd.edu)

Current Opinion in Neurobiology 2006, **16**:1–10

This review comes from a themed issue on
Sensory systems
Edited by Yang Dan and Richard D Mooney

0959-4388/$ – see front matter
© 2006 Elsevier Ltd. All rights reserved.

DOI 10.1016/j.conb.2006.06.009

Introduction

Active touch is a common behavior that animals use to discern the shape, size and texture of objects. The resulting haptic sensations are used to finely tune the position or the motion of tactile sensors. The transformation of sensory inputs into modulatory motor outputs during active touch is performed by sensorimotor feedback loops [1]. Here, we discuss active touch in the context of rhythmic, 5 to 25 Hz whisking by the rat [2] (Figure 1). These animals palpate objects with their vibrissae during a bout (see glossary) of whisking, which lasts for one second or more, to extract a stable picture of the world.

Can rats discriminate objects solely with their vibrissae?

Hutson and Masterton [3] devised sensory tests to isolate perceptual functions of the vibrissae. They found that blind rats with intact vibrissae would leap across wide gaps after contacting the opposite platform with their vibrissae. Rats with clipped vibrissae did not cross these wide gaps. Thus, sensory input from vibrissae enables animals to determine the existence and location of the far side of a gap, in a process that is well suited for electrophysiological studies [4,5]. A complementary role for the involvement of the vibrissae in detection tasks follows from studies on the discrimination of different textures, in which it is conjectured that rats discriminate with an acuity that rivals that of the human fingertip [6].

Texture is not the only fine sense transduced by the vibrissae. Recent experiments suggest that the vibrissae convey sufficient spatial information to enable rats to distinguish between differently shaped objects [7,8] and between alleys that differ in width by less than five percent [9,10].

Background

The rat vibrissa sensorimotor system consists of nested feedback loops

The vibrissae are embedded in feedback loops that form a closed topology at the level of brainstem up through loops that close at the level of the neocortex [11] (Figure 2). Our thesis is that these loops mediate active sensing, which involves a confluence of neuronal signals that represent touch with those that represent vibrissa position.

The brainstem sensorimotor loop is the lowest-order circuit in which sensorimotor integration occurs [12,13]. It contains secondary sensory nuclei as well as the motor nuclei that control motion of each vibrissa [14] through both intrinsic muscles in the mystacial pad (see glossary) and extrinsic muscles that move the pad as a whole [15]. These movements work in opposition to ensure active protraction and retraction in the whisk cycle (see glossary) [2,16]. The brainstem loop is believed to participate in rhythmic pattern generation [17•,18], based on evidence that whisking persists after lesions to vibrissae-related areas of neocortex [19,20] and the cerebellum [20], although the location of a central pattern generator in the brainstem in unknown.

The background firing-rate of motoneurons in the lateral aspect of the facial nucleus, which innervates the intrinsic muscles [21,22], depends on modulation by serotonergic neurons [18]. This modulation is analogous to the control of posture by spinal neurons [23] and, thus, probably controls the set-point (see glossary) of the vibrissae. We conjecture that the interplay between motoneurons in the medial aspect of the facial nucleus, which innervates the extrinsic muscles [14], and those in the lateral

Glossary

Artificial whisking:: A technique to drive vibrissa motion in the anesthetized animal through electrical stimulation of the relevant branch(es) of the facial nerve.

Barrels: Dense clusters of cell bodies, largely stellate neurons, in layer 4 of vibrissa primary sensory cortex. The clusters are arranged in a one-to-one map of the vibrissae and each cluster receives a dense projection from topographically matched cell cluster in ventral posterial medial (VPM-dm) thalamus.

Bout: The succession of whisks that last 1 to 4 seconds, over which the frequency of whisking could be well defined.

Exploratory whisking: Rhythmic, large amplitude forward and backward sweeps of the vibrissae around a set-point, with frequencies in the range of 5 to 15 Hz.

Foveal whisking: Rhythmic, small amplitude sweeps of the vibrissae, with the vibrissae thrust forward, with frequencies in the range of 15 to 25 Hz.

Mystacial pad: The area of the cheek that hosts the vibrissae that is richly innervated by motor and sensory terminations.

Phase-locking: The tracking of one signal by another, in which the frequencies are equalized and, on average, a constant phase difference is maintained.

Q-factor: A measure of the damping of a resonant oscillator that nominally corresponds to the number of cycles required for the amplitude to decrease to 1/e of its initial value.

Septa: The tissue between the barrels in layer 4 of vibrissa primary sensory cortex.

Servo control: A feedback scheme to maintain the output of a signal, for example, the amplitude or the frequency, formed upon the basis of comparison with a reference signal.

Set point: The angle around which whisking is centered.

Triangulation: A method to localize a target based on an intersection of azimuths from two (or more) sources.

Vibrissae: The long hairs, properly called the macrovibrissae, that protrude from the mystacial pad and are used to palpate objects. Vibrissae are also referred to as 'whiskers'.

Weber's Law: A logarithmic relation between the physical intensity of a stimulus and the perception (and implicitly the neuronal coding) of that intensity.

Whisk cycle: One cycle of vibrissa movement that includes a protraction phase followed by a retraction phase.

aspect of the nucleus could be crucial for the control of whisking strategy, such as the change from large exploratory whisks to foveal whisks (see glossary) in the palpation of objects [2].

The midbrain, thalamic and cortical loops provide feedback pathways that parallel the monosynaptic pathway from the trigeminal nuclei to the facial nucleus (Figure 2) [24,25]. Three such pathways involve thalamic nuclei. The first is an extralemniscal pathway that ascends through the ventrolateral sector of ventral posterior medial (VPM-vl) thalamus to vibrissa primary sensory (S1) and secondary sensory (S2) cortex [26]. The second is a paralemniscal pathway that passes through posterior medial (POm) thalamus and projects down to the superior colliculus as well as up to S1, S2 and primary motor (M1) cortices [27–29]. The third is a lemniscal pathway that passes through the dorsomedial sector of ventral posterior medial (VPM-dm) thalamus to vibrissa S1 cortex. The extralemniscal pathway conveys primarily touch-based signals, the paralemniscal pathway conveys primarily vibrissa motion signals, which can be used to form positional reference signals, and the lemniscal pathway conveys a combination of touch and motion signals [30•]. Despite this segregation of information, the thalamic nuclei interact through reciprocal connections to the reticular thalamic nucleus (Rt) [31,32], which can shape their dynamic response [33]. Furthermore, the pattern of corticothalamic descending connections [34,35] mirrors that of trigeminothalamic ascending inputs [28,36], a scheme that enables the thalamus to compare top-down predictions with sensory input [37].

Sensory and motor cortices interact through corticocortical projections and through thalamic-mediated connections among these cortical areas, principally involving POm thalamus [33–40] (Figure 2). This organization implies that the computations involved in sensory and motor functions are likely to be distributed throughout these cortical and thalamic areas [41]. Interestingly, the lemniscal pathway could suppress activity in the paralemniscal pathway through cortical activation of cells in the zona incerta [42,43], a process that is partially suppressed when animals are in the aroused state [44]. Activation of cells in the zona incerta subsequently inhibits neurons in POm thalamus [45,46,47•]. Thus, corticothalamic feedback from sensory cortex could gate the input of trigeminal sensory information to motor cortex. Nonetheless, the means by which neuronal activity in cortex can control information in ascending vibrissa pathways has only just begun to be addressed [48].

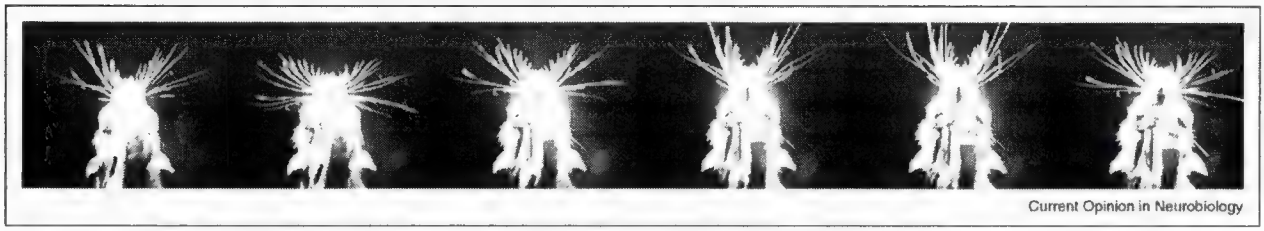
The neocortical loop is completed by projections from M1 cortex to the vibrissa areas of the facial nucleus [49•] as well as to other brainstem nuclei that connect to the facial nucleus [50,51]. Furthermore, projections from both S1 and M1 cortices to the superior colliculus are transformed into descending projections to the facial nucleus (Figure 2). A crucial question is how vibrissa motoneurons, which preferentially spike for transient inputs in the frequency range of natural whisking [52], merge inputs from brainstem, midbrain, thalamic and cortical feedback loops.

Object localization and vibrissa movement

Active vibrissa movements in free-ranging animals are always associated with active head and body movements. When rats are engaged in a horizontal localization task, in which they estimate the location of objects relative to their head in the azimuthal plane, they typically whisk [53]. However, whisking is not always necessary for vibrissa-based tactile sensation, as rats often rely solely on passive movement of the vibrissae secondary to body and head movements. In particular, rats use their vibrissae but do not whisk as they maintain contact with walls and surfaces [54] while running and while performing an aperture-size discrimination task [9].

The necessity and pattern of whisking could depend on the geometrical arrangement of the vibrissae. The altitude of an object can, in principle, be determined if the animal

Figure 1

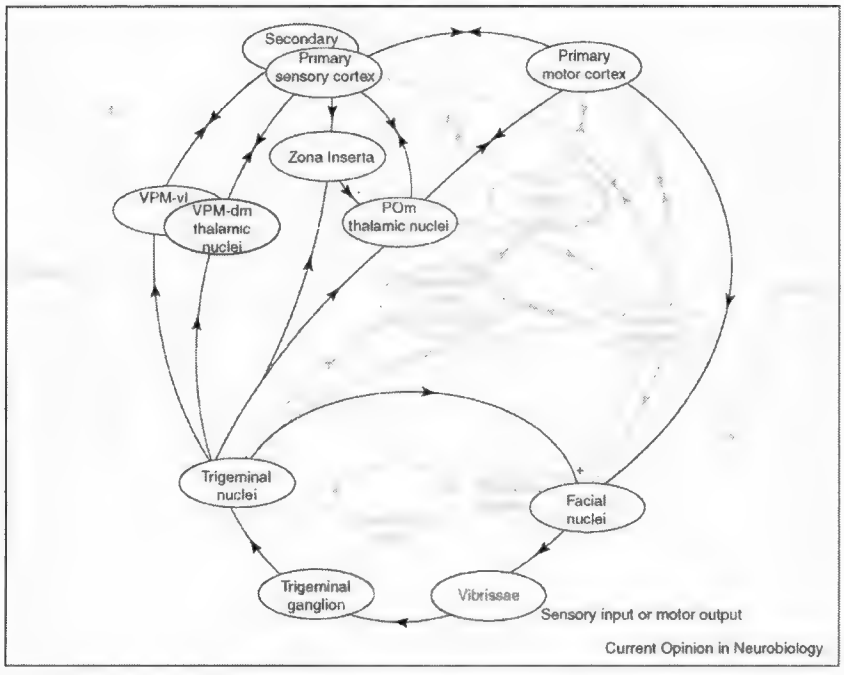


Successive strobed video images of a rat, using darkfield illumination from above, as she moves her vibrissae during a whisk cycle. The animal was trained, while blindfolded, to whisk in search of a food tube (not shown). Successive frames are at intervals of 33 ms. Data obtained as part of the study by Fee *et al.* [73].

senses which of the five possible rows of vibrissae the object is in contact with. The rows span $\sim 100^\circ$ range from contact with the ground to contact with objects above the head [55]. Thus, movement of the vibrissae is not necessary to assess altitude, but small movements can be used to locate objects on a scale finer than the $\sim 25^\circ$ spacing. In contrast to altitude determination, the $\sim 75^\circ$ span among the ~ 6 long vibrissae in a row covers less than a half of a hemifield in the azimuthal plane [21], so complete coverage of the sensory field requires that the vibrissa sweep along the anterior–posterior axis. The range of exploratory whisking is consistent with this coverage and further includes limited movement in the dorsal–ventral direction to increase the resolution of altitude [56].

The distance of an object from the face is coded by a firing rate that appears to be independent of the azimuthal position of the vibrissa [57]. Thus, a reference of vibrissa position is not needed to specify this distance, which coincides with the radial coordinate of contact along the vibrissa with the follicle pore taken as the origin. A similar argument exists for the altitude of an object. By contrast, a

Figure 2



Simplified cartoon of the topologically nested vibrissa sensorimotor loops. The brainstem and thalamocortical pathways covered in this review are shown with black lines. Cerebellar pathways are shown in gray, whereas those that involve basal ganglia [114–116] are not shown. A complete description and a full set of references are found in Kleinfeld *et al.* [11]. Here, we have added a positive feedback connection (+) at the brainstem level [17•], a negative feedback connection (–) from zona incerta to POm thalamus [42,43], the division of VPM thalamus into dorsal medial (dm) and ventral lateral (vl) areas [26,30•], and a connection form POm thalamus to the superior colliculus [27].

reference of vibrissa position is essential to code the azimuth of contact as the vibrissae sweep along the anterior–posterior axis. Crucially, the pressure receptors in the follicle [58,59] respond to vibrissa contact in a manner consistent with compression of the follicle by motion that is predominantly along the azimuthal coordinate.

Coding rhythmic sensory signals

Common scaling for the cortical spike-rate

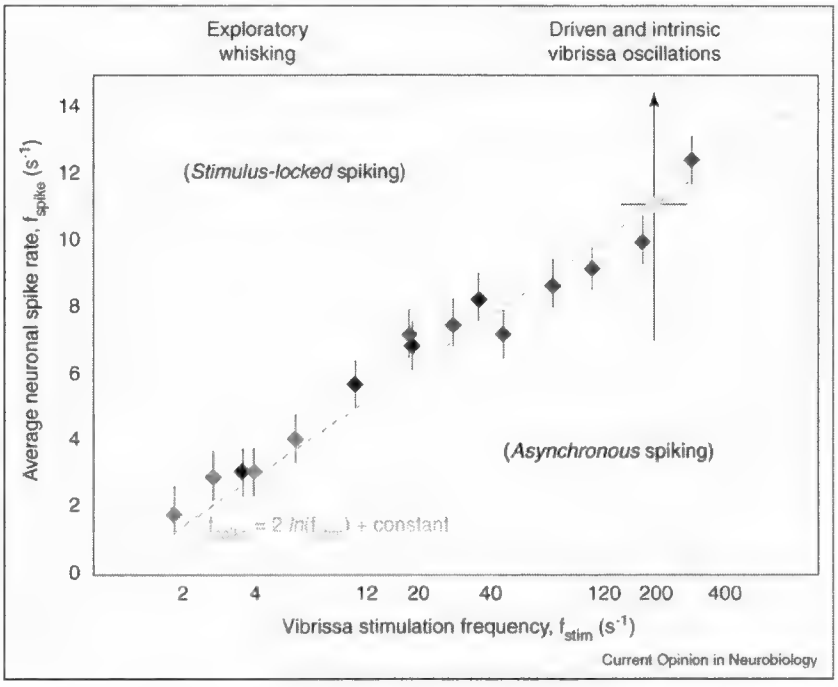
Here, we have grouped discrimination tasks into two classes. The first class concerns searching for and palpating edges and objects, for which animals exhibit large-angle exploratory whisking in the range of 5 to 15 Hz and foveal whisking up to 25 Hz [2]. Crucially, neurons throughout the entire sensory stream can follow with spike-by-spike precision at these frequencies [60,61], so that touch signals can be accurately timed relative to the position of the vibrissae. The second class concerns differentiation among textures, during which the vibrissae can vibrate at hundreds to thousands of Hertz as they sweep across a surface [62,63]. These high frequency signals are faithfully represented in the trigeminal nucleus [64,65]. However, cortical cells do not to follow inputs at such high frequency, although cortical oscillations at hundreds of Hertz, unrelated to texture, are documented [66,67]. It is thus of interest that high frequency signals are represented in cortex as an irregular spiking process in which the spike rate is a monotonic function of the rate of stimulation [68•,69].

Independent of the task and the phase-coherence between the sensory stimulation and the spike response in cortex, the stimulus is coded by logarithmic compression of the stimulation frequency (Figure 3). This universal representation is analogous to Weber's Law (see glossary) for the peripheral nervous system, with stimulus frequency replacing stimulus intensity. Phase-locking (see glossary) occurs for exploratory whisking, a strategy involved in object location, whereas an absence of locking is associated with texture discrimination. More refined analyses show that distinct temporal patterns of spikes emerge with textures of similar coarseness but differing details [68•], and that increases in firing rate with increasing stimulation frequency are primarily confined to neurons in the regions, denoted septa (see glossary), between cortical columns [70].

Active touch for object recognition and path finding

The essential issue in localization of an object in the azimuthal plane is to transform a touch signal into a measure of the angle relative to the face. In principle, this can be accomplished by contacting the object with an

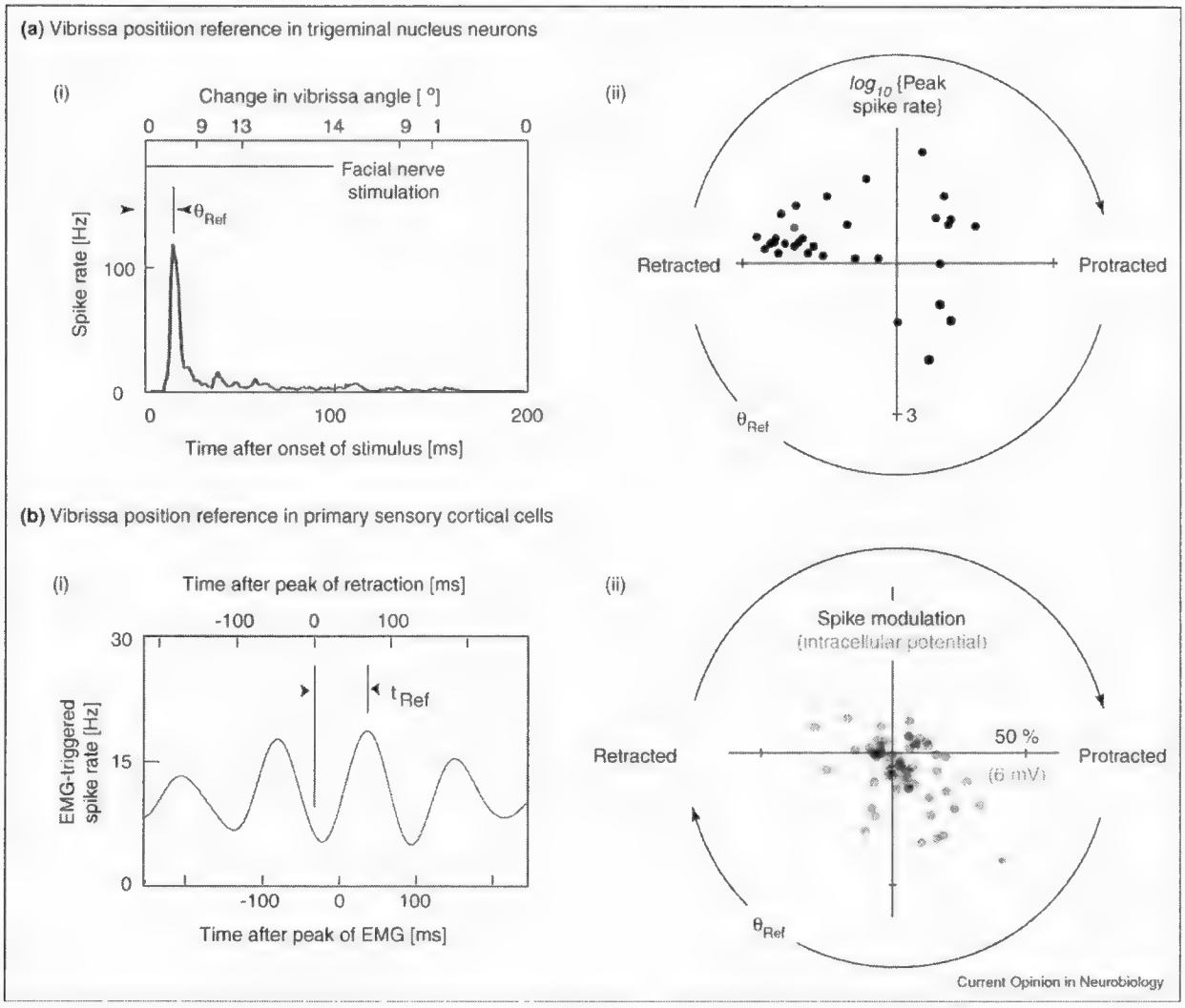
Figure 3



Coding of rhythmic vibrissa stimulation in S1 cortex of anesthetized animals. The data represent a composite extracted from the published results from multiple laboratories; green diamonds from Ahissar *et al.* [88], purple from Khatri *et al.* [117]; red from Arabzadeh *et al.* [68•], and blue from Andermann *et al.* [98]. Note that the results from Arabzadeh *et al.* [68•] are for a particular rhythmic amplitude; other angular speeds (speed = amplitude × frequency) with the same frequency are offset by a constant. The slope of the response across all data sets can be approximated by logarithmic scaling, as indicated by the dashed line and proposed on theoretical grounds [118].

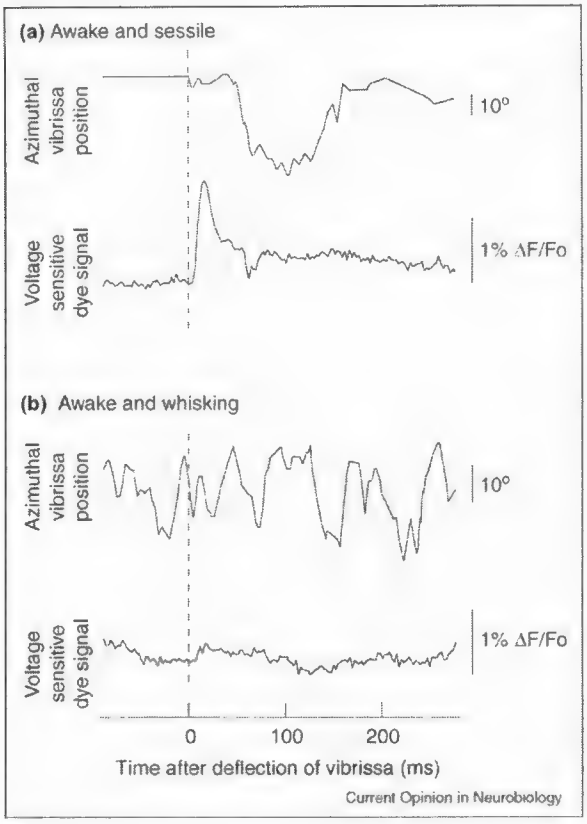
array of vibrissae, together with triangulation (see glossary) [62], or by contacting the object with a single vibrissa and combining the touch signal with a reference signal of vibrissa position. New behavioral experiments are required to distinguish between these possibilities. Nonetheless, electrophysiological studies support the presence of a neuronal reference of vibrissa position. First, signals of vibrissa touch, as well as signals of vibrissa motion that are appropriate reference signals, exist at the level of the trigeminal ganglion [71] (Figure 4a). Second, both active touch signals [72•] and reference signals [73,74•] (Figure 4b) are present in S1 cortex. Interestingly, the touch response is suppressed during whisking, at least as assayed in mice [72•] (Figure 5), consistent with both adaptation of the cortical response that occurs secondary to suppression of thalamocortical synaptic transmission in the aroused state [75,76] and possible gating by motor activity [77,78]. Furthermore, the reliability of the

Figure 4



Encoding of vibrissa position. **(a)** Spiking output from primary sensory neurons of the trigeminal ganglion (TG) was recorded during vibrissa motion induced by 5 Hz electrical stimulation of the facial motor nerve (FN). **(i)** The trial-averaged response of the reference signal for one neuron; the angle $\Delta\theta_{Ref}$ is the extent of protraction, relative to the initial retracted position, at the peak of the neuronal response. **(ii)** The summarized data for all cells [71]. The radial polar coordinate is the logarithm of the peak spike rate and the angular polar coordinate is the phase within the whisk cycle. **(b)** Responses in vibrissa S1 cortex measured while animals whisked without contact. **(i)** An example of the correlation between spiking and the peak of the electromyogram (EMG). The scale across the top accounts for the lag between vibrissa position and the EMG [2]; the time t_{Ref} is the peak of cortical spiking relative to the fully retracted position. **(ii)** Summarized data for all cells [62,73] from these extracellular measurements, for which the radial coordinate is the modulation of the spike–EMG correlation, as well as for cells from recent intracellular studies [74•], for which the radial coordinate is the maximum intracellular depolarization. The bias in spiking as a function of phase in the whisk cycle comes slightly earlier than that for the membrane depolarization, as expected for a threshold process.

Figure 5



The evoked sensory response in awake mice depends strongly on behavior [72•]. **(a)** The positional plot shows the measured change in azimuthal displacement. The voltage sensitive dye signal measures the average membrane potential within the focal volume and is reported as the fraction change in fluorescence ΔF/Fo. The dye signal shows a large amplitude response following transient magnetically induced displacement of the altitude of vibrissa C2, which served as the stimulus. Note that approximately 70 ms after this cortical response the mouse protracted its vibrissa. The scale ΔF/Fo refers to the fraction change in optical signal. **(b)** The dye signal of the mouse during active whisking when the magnetic deflection was applied. A much smaller sensory response was observed.

cortical reference signal is strongly enhanced when whisking is paired with reward [79]. Details aside, a nonlinear interaction between touch and reference signals, for example correlation, is sufficient to compute object location with single-vibrissa resolution in face centered coordinates. Evidence for an appropriate nonlinearity in S1 cortex exists [80,81]. Yet, a position-dependent touch signal remains to be demonstrated.

How are active touch signals processed in a cortical column? To answer this question, we consider experiments that used artificial whisking (see glossary) [82] to generate a sensory signal. The responses of neurons in the 'barrel' (see glossary) regions within layer 4 [83], which receive lemniscal (VPM-dm) input (Figure 2), in addition to those in layer 5a, which receive paralemniscal (POm) input, are facilitated with successive whisks [84]. The facilitation in layer 4 neurons is stronger when contact occurs during whisking, whereas responses in layer 5a neurons are usually unaffected by contact. By contrast, the responses in superficial layer 2/3 neurons, which mediate intercolumnar interactions [85], are depressed with repetitive contact [84]. These differences in cortical dynamics across laminae are suggestive of specialized processing within different layers [86] that relates to the associated afferent pathway [87–89]. Layer 4 neurons are posited to process spatial details of the palpated object, for which their columnar segregation [90] is consistent with single-vibrissa spatial resolution. By contrast, layer 5a neurons process vibrissa position and whisking kinematics. We thus hypothesize the existence of integration across neighboring columns within layer 5a [91•]. Finally, layer 2/3 neurons appear to integrate the outputs of layers 4 and 5a [88,92•]. The role of arousal [75,76] and adaptation [93,94] in this cortical computation remains to be evaluated.

From mechanics to spiking in texture discrimination

There are two current hypotheses on the mechanical origin of high frequency trigeminal signals that accompany texture discrimination tasks [63,95]. The first hypothesis involves mechanical resonance of the vibrissae [96,97] and is applicable when the drag on the vibrissa does not induce appreciable damping of the motion. This hypothesis originates from the observation that whiskers within a vertical arc, for example A2 through E2, are of similar length, whereas whiskers along a row, for example D1 through D6, decrease in length in the posterior–anterior dimension [7]. As a consequence, the longer, posterior vibrissa should exhibit a resonance with lower fundamental frequencies than the shorter, anterior vibrissae [95]. According to this hypothesis, as the vibrissae sweep along a textured surface, the vibrissa the resonance frequency of which most closely matches the texture-induced input frequency will transmit the greatest torque to the follicle [98]. Thus, an increase in firing rate at a specific position within the map of vibrissa position in S1 cortex would indicate the predominant frequency of whisker vibration and, consequently, the identity of the contacted texture [63]. Consistent with the predictions of the resonance hypothesis, vibrissae are observed to resonate when complex textures, such as sandpaper, are translated across the tip of the vibrissa [99]. The spike activity of neurons in the afferent pathway rises over a period of ~500 ms, consistent with the Q-factor (see glossary) of the resonance [98], so that coding of textures by the rate of spiking is probably relevant when many arcs of vibrissae sweep the texture for an extended period of time [100].

The second hypothesis is that contact of the vibrissae with a surface is dominated by damping. In this hypothesis, resonant vibrations are suppressed while vibrations that reflect the topology of the surface dominate the stimulus-

induced motion of the vibrissa [68•]. Thus, the spatial modulation of the surface is reproduced by the pattern of spiking in trigeminal ganglion neurons. Experiments that used artificial whisking in the anesthetized animal provide proof-of-principle demonstration of this scheme [68•]. Distinguishing between these two coding strategies — one in which the underlying frequency components depend on intrinsic mechanical properties and the other in which the components depend upon extrinsic properties — will require quantification of vibrissa kinematics and associated neuronal activity while rats explore textured surfaces.

Sensory modulation of vibrissa motion

Although anecdotal evidence exists for changes in whisking strategy on the basis of the discrimination task [2,6,101,102], there is a paucity of quantitative data on both the psychophysics and the electrophysiology of sensory control of motor output. Nonetheless, recent work shows that the brainstem loop exerts transient positive feedback [17•] (Figure 2), such that the initiation of touch leads to a protracted period of contact [103]. This mechanism might increase the number of contact-mediated spikes and thus the reliability of a touch signal.

We conjecture that changes in whisking strategies are regulated at the corticothalamic level. Three classes of recent experiments support this view. A first class of experiments made use of awake, head-fixed animals that were trained not to whisk as a means to delineate the representation of rhythmic sensory input within M1 cortex [41]. Surprisingly, the observed response captured only the fundamental frequency of the input pattern for pulsatile stimuli with frequencies ranging from 5 to 20 Hz, the range of exploratory whisking. This nonlinear transformation resembles the synthesis of a sinusoidal feedback signal for servo-control (see glossary) of a motor.

A second class of experiments showed that M1 cortex supports oscillations in extracellular current-flow that are phase-locked to whisking as animals whisk in air [104]. These signals are preserved after lesions of the infraorbital branch of the trigeminal nerve block sensory input. Furthermore, ablation of M1 cortex leads to alteration of the whisking patterns [105]. Thus, motor cortex generates rhythmic signals that can drive normal exploratory whisking.

The third and final class of experiments built on early work by Welker and co-workers [106] and explored the motion of the vibrissa in response to activation of M1 cortex in both anesthetized and behaving animals. From a functional perspective, there are two contiguous motor areas [107•]. For the largest region, denoted 'retraction-face' (RF), activation of tissue with a brief train of extracellular current-pulses [107•,108], or even depolarization of a single cell [109,110], leads to retraction of the vibrissae. This motion is transformed into a full whisk, with protraction and retraction, when animals are in the awake and aroused state [108], an effect that is mimicked by cholinergic activation of cortex [111•]. Furthermore, the induction of 5 to 15 Hz oscillations in motor cortex through pharmacologically induced disinhibition leads to cycles of retraction that are phase-locked to the cortical rhythm [112]. A similar effect occurs in response to prolonged electrical excitation to motor cortex [113]. For a smaller region near the midline, denoted 'rhythmic whisking' (RW), activation with a brief train of extracellular current-pulses leads to protraction [107•]. Rather remarkably, stimulation of the RW region in the awake animal, using a continuous train of high-frequency pulses, induces lower frequency rhythmic whisking [107•]. The set-point of whisking can be varied by simultaneous activation of the RF and RW regions. Collectively, these data show that M1 cortex, in principle, can subsume full control of vibrissa movement.

Conclusions

An analysis of the available data is consistent with the notion of motor control of the vibrissae by sensorimotor loops at the brainstem through cortical levels. Although neural correlates of vibrissa position and touch are already present in the brainstem loop, it appears that the convergence of these signals for object discrimination first occurs within sensory cortex, where we posit that representations of vibrissa position fuse with those of object contact. The available data further imply that rhythmic drive to the vibrissae can be under the control of motor cortex during active sensing. We thus hypothesize that the processed sensory stream is used to assess whisking strategy continuously and modify whisking on both cycle-by-cycle and bout-to-bout time-scales. To the extent that changes in motor drive can coincide with object identification, it might be useful to think of motor control as a 'read out' from sensory cortex.

Acknowledgements

We thank the Human Frontiers Scientific Program (ME Diamond, D Kleinfeld and E Ahissar), the US-Israeli Binational Science Foundation (E Ahissar and D Kleinfeld), the Center for Theoretical Biological Physics with funding from the National Science Foundation (D Kleinfeld), the Benign Essential Blepharospasm Foundation (D Kleinfeld), the European Community Information Society Technologies Framework Program (ME Diamond), the Telethon Foundation (ME Diamond), the Ministero per l'Istruzione, l'Università e la Ricerca (ME Diamond), the Israel Science Foundation (E Ahissar), and the Minerva Foundation with funding from the Federal German Ministry for Education and Research (E Ahissar) for financial support, and D Hill and M Szwed for comments on early versions of the article.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Ahissar E, Kleinfeld D: **Closed loop neuronal computations: focus on vibrissa somatosensation in rat.** *Cereb Cortex* 2003, **13**:53-61.

2. Berg RW, Kleinfeld D: **Rhythmic whisking by rat: Retraction as well as protraction of the vibrissae is under active muscular control**. *J Neurophysiol* 2003, **89**:104-117.

3. Hutson KA, Masterton RB: **The sensory contribution of a single vibrissa's cortical barrel**. *J Neurophysiol* 1986, **56**:1196-1223.

4. Sachdev RN, Egli M, Stonecypher M, Wiley RG, Ebner FF: **Enhancement of cortical plasticity by behavioral training in acetylcholine-depleted adult rats**. *J Neurophysiol* 2000, **84**:1971-1981.

5. Harris JA, Petersen RS, Diamond ME: **Distribution of tactile learning and its neutral basis**. *Proc Natl Acad Sci USA* 1999, **96**:7587-7591.

6. Carvell GE, Simons DJ: **Task-and subject-related differences in sensorimotor behavior during active touch**. *Somatosens Mot Res* 1995, **12**:1-9.

7. Brecht M, Preilowski B, Merzenich MM: **Functional architecture of the mystacial vibrissae**. *Behav Brain Res* 1997, **84**:81-97.

8. Harvey MA, Bermejo R, Zeigler HP: **Discriminative whisking in the head-fixed rat: optoelectronic monitoring during tactile detection and discrimination tasks**. *Somatosens Mot Res* 2001, **18**:211-222.

9. Krupa DJ, Matell MS, Brisben AJ, Oliveira LM, Nicolelis MAL: **Behavioral properties of the trigeminal somatosensory system in rats performing whisker-dependent tactile discriminations**. *J Neurosci* 2001, **21**:5752-5763.

10. Shuler MG, Krupa DJ, Nicolelis MA: **Integration of bilateral whisker stimuli in rats: role of the whisker barrel cortices**. *Cereb Cortex* 2002, **12**:86-97.

11. Kleinfeld D, Berg RW, O'Connor SM: **Anatomical loops and their electrical dynamics in relation to whisking by rat**. *Somatosens Mot Res* 1999, **16**:69-88.

12. Kis Z, Rakos G, Farkas T, Horvath S, Toldi J: **Facial nerve injury induces facilitation of responses in both trigeminal and facial nuclei of rat**. *Neurosci Lett* 2004, **358**:223-225.

13. Erzurumlu RS, Killackey HP: **Efferent connections of the brainstem trigeminal complex with the facial nucleus of the rat**. *J Comp Neurol* 1979, **188**:75-86.

14. Klein B, Rhoades R: **The representation of whisker follicle intrinsic musculature in the facial motor nucleus of the rat**. *J Comp Neurol* 1985, **232**:55-69.

15. Bermejo R, Friedman W, Zeigler HP: **Topography of whisking II: interaction of whisker and pad**. *Somatosens Mot Res* 2005, **22**:213-220.

16. Shaw FZ, Liao YF: **Relation between activities of the cortex and vibrissae muscles during high-voltage rhythmic spike discharges in rats**. *J Neurophysiol* 2005, **93**:2435-2448.

17. • Nguyen QT, Kleinfeld D: **Positive feedback in a brainstem tactile sensorimotor loop**. *Neuron* 2005, **45**:1-11.
The authors describe the closed loop dynamics of the vibrissa to trigeminal ganglion, to trigeminal nucleus, to facial motor nucleus, to vibrissa loop using brainstem slice and *in vivo* preparations. This is the first report on signaling in a closed sensorimotor loop outside of the spinal reflex arc.

18. Hattox A, Li Y, Keller A: **Serotonin regulates rhythmic whisking**. *Neuron* 2003, **39**:343-352.

19. Gao P, Bermejo R, Zeigler HP: **Vibrissa deaffentation and rodent whisking patterns: behavioral evidence for a central pattern generator**. *J Neurosci* 2001, **21**:5374-5380.

20. Welker WI: **Analysis of sniffing of the albino rat**. *Behaviour* 1964, **12**:223-244.

21. Wineski LE: **Facial morphology and vibrissal movement in the golden hamster**. *J Morphol* 1985, **183**:199-217.

22. Dorfl J: **The innervation of the mystacial region of the white mouse. A topographical study**. *J Anat* 1985, **142**:173-184.

23. Growdon JH: **Changes in motor behavior following the administration of serotonin neurotoxins**. *Ann N Y Acad Sci* 1978, **305**:510-523.

24. Alonso JM, Swadlow HA: **Thalamocortical specificity and the synthesis of sensory cortical receptive fields**. *J Neurophysiol* 2005, **94**:26-32.

25. Jones EG, Diamond IT: **Cerebral Cortex: Volume 11: The Barrel Cortex of Rodents**Springer; 1995.

26. Pierret T, Lavallee P, Deschenes M: **Parallel streams for the relay of vibrissal information through thalamic barreloids**. *J Neurosci* 2000, **20**:7455-7462.

27. Cadusseau J, Roger M: **Distribution of the efferent projections of the rat posterior thalamic nucleus as revealed by phaseolus vulgaris immunohistochemistry**. *J Himforsch* 1990, **31**:459-465.

28. Diamond ME, Armstrong-James M, Ebner FF: **Somatic sensory responses in the rostral sector of the posterior group (POm) and in the ventral posterior medial nucleus (VPM) of the rat thalamus**. *J Comp Neurol* 1992, **318**:462-476.

29. Ahissar E, Sosnik R, Haidarliu S: **Transformation from temporal to rate coding in a somatosensory thalamocortical pathway**. *Nature* 2000, **406**:302-306.

30. • Yu C, Derdikman D, Haidarliu S, Ahissar E: **Parallel thalamic pathways for whisking and touch signals in the rat**. *PLoS Biol* 2006, **4**:e124.
The authors report on segmentation of function among the three thalamic pathways conveying active touch signals. The paralemniscal pathway conveys whisking (reference) signals, the extralemniscal pathway conveys contact signals, and the lemniscal pathway conveys complex whisking-touch signals.

31. Crabtree JW, Isaac JT: **New intrathalamic pathways allowing modality-related and cross-modality switching in the dorsal thalamus**. *J Neurosci* 2002, **22**:8754-8761.

32. Crabtree JW, Collingridge GL, Isaac JT: **A new intrathalamic pathway linking modality-related nuclei in the dorsal thalamus**. *Nat Neurosci* 1998, **1**:389-394.

33. Golomb D, Ahissar E, Kleinfeld D: **Coding of stimulus frequency by latency in thalamic networks through the interplay of $GABA_B$-mediated feedback and stimulus shape**. *J Neurophysiol* 2005, **95**:1735-1750.

34. Reichova I, Sherman SM: **Somatosensory corticothalamic projections: distinguishing drivers from modulators**. *J Neurophysiol* 2004, **92**:2185-2197.

35. Temereanca S, Simons DJ: **Functional topography of corticothalamic feedback enhances thalamic spatial response tuning in the somatosensory whisker/barrel system**. *Neuron* 2004, **41**:639-651.

36. Deschenes M, Veinante P, Zhang Z-W: **The organization of cortico-thalamic pathways: reciprocity versus parity**. *Brain Res Brain Res Rev* 1998, **28**:286-308.

37. Ahissar E, Haidarliu S, Zacksenhouse M: **Decoding temporally encoded sensory input by cortical oscillations and thalamic phase comparators**. *Proc Natl Acad Sci USA* 1997, **94**:11633-11638.

38. Hoffer ZS, Arantes HB, Roth RL, Alloway KD: **Functional circuits mediating sensorimotor integration: quantitative comparisons of projections from rodent barrel cortex to primary motor cortex, neostriatum, superior colliculus, and the pons**. *J Comp Neurol* 2005, **488**:82-100.

39. Hoffer ZS, Hoover JE, Alloway KD: **Sensorimotor corticocortical projections from rat barrel cortex have an anisotropic organization that facilitates integration of inputs from whiskers in the same row**. *J Comp Neurol* 2003, **466**:525-544.

40. Veinante P, Deschenes M: **Single-cell study of motor cortex projections to the barrel field in rats**. *J Comp Neurol* 2003, **464**:98-103.

41. Kleinfeld D, Sachdev RNS, Merchant LM, Jarvis MR, Ebner FF: **Adaptive filtering of vibrissa input in motor cortex of rat**. *Neuron* 2002, **34**:1021-1034.

42. Power BD, Kolmac CI, Mitrofanis J: **Evidence for a large projection from the zona incerta to the dorsal thalamus**. *J Comp Neurol* 1999, **404**:554-565.

43. Chapin JK, Schneider JS, Nicolelis M, Lin C-S: **A major direct GABAergic pathway from zona incerta to neocortex**. *Science* 1990, **248**:1553-1556.

44. Trageser JC, Burke KA, Masri R, Li Y, Sellers L, Keller A: **State-dependent gating of sensory inputs by zona incerta.** *J Neurophysiol* 2006. In press.

45. Bartho P, Freund TF, Acsady L: **Selective GABAergic innervation of thalamic nuclei from zona incerta**. *Eur J Neurosci* 2002, **16**:999-1014.

46. Trageser JC, Keller A: **Reducing the uncertainty: gating of peripheral inputs by zona incerta**. *J Neurosci* 2004, **24**:8911-8915.

47. • Lavallee P, Urbain N, Dufresne C, Bokor H, Acsady L, Deschenes M: **Feedforward inhibitory control of sensory information in higher-order thalamic nuclei**. *J Neurosci* 2005, **25**:7489-7498.
The authors expose a link, via zona incerta, by which the lemniscal pathway can inhibit the paralemniscal pathway through feedback from sensory cortex. Importantly, the difference in response between VPM and POm thalamic nuclei is not attributable to differences in trigeminal afferent strength, but to this efficient feedforward inhibition.

48. Hentschke H, Haiss F, Schwarz C: **Central signals rapidly switch tactile processing in rat barrel cortex during whisker movements.** *Cereb Cortex* 2006. in press.

49. • Grinevich V, Brecht M, Osten P: **Monosynaptic pathway from rat vibrissa motor cortex to facial motor neurons revealed by lentivirus-based axonal tracing**. *J Neurosci* 2005, **25**:8250-8258.
The authors pioneer the use of viral agents for track-tracing in motor systems. They show that cortical units make direct connections to vibrissa motoneurons, in analogy with the corticospinal track.

50. Hattox AM, Priest CA, Keller A: **Functional circuitry involved in the regulation of whisker movements**. *J Comp Neurol* 2002, **442**:266-276.

51. Miyashita E, Keller A, Asanuma H: **Input-output organization of the rat vibrissal motor cortex**. *Exp Brain Res* 1994, **99**:223-232.

52. Nguyen Q-T, Wessel R, Kleinfeld D: **Developmental regulation of active and passive membrane properties in rat vibrissa motoneurones**. *J Physiol* 2004, **556**:203-219.

53. Knutsen PM, Derdikman D, Ahissar E: **Tracking whisker and head movements in unrestrained behaving rodents.** *J Neurophysiol* 2005, **93**:2294-2301.

54. Milani H, Steiner H, Huston JP: **Analysis of recovery from behavioral asymmetries induced by unilateral removal of vibrissae in the rat**. *Behav Neurosci* 1989, **103**:1067-1074.

55. Wineski LE: **Movements of the cranial vibrissae in the golden hamster (mesocritus auratus)**. *J Zool* 1983, **200**:261-280.

56. Bermejo R, Vyas A, Zeigler HP: **Topography of rodent whisking I. two-dimensional monitoring of whisker movements**. *Somatosens Mot Res* 2002, **19**:341-346.

57. Szwed M, Bagdasarian K, Blumenfeld B, Barak O, Derdikman D, Ahissar E: **Responses of trigeminal ganglion neurons to the radial distance of contact during active vibrissal touch**. *J Neurophysiol* 2006, **95**:791-802.

58. Rice FL, Fundin BT, Arvidsson J, Aldskogius H, Johansson O: **Comprehensive immunofluoresce and lectin binding study of the innervation of vibrissae follicle sinus complexes on the mystacial pad of the rat**. *J Comp Neurol* 1997, **385**:149-184.

59. Leiser SC, Moxon KA: **Relationship between physiological response type (RA and SA) and vibrissal receptive field of neurons within the rat trigeminal ganglion**. *J Neurophysiol* 2006, **95**:3129-3145.

60. Deschenes M, Timofeeva E, Lavallee P: **The relay of high frequency sensory signals in the whisker-to-barreloid pathway**. *J Neurosci* 2003, **23**:6778-6787.

61. Hartings JA, Temereanca S, Simons DJ: **Processing of periodic whisker deflections by neurons in the ventroposterior medial and thalamic reticular nuclei**. *J Neurophysiol* 2003, **90**:3087-3094.

62. Mehta SB, Kleinfeld D: **Frisking the whiskers: patterned sensory input in the rat vibrissa system**. *Neuron* 2004, **41**:181-184.

63. Moore CI: **Frequency-dependent processing in the vibrissa sensory system**. *J Neurophysiol* 2004, **91**:2390-2399.

64. Gottschaldt KM, Iggo A, Young DW: **Electrophysiology of the afferent innervation of sinus hairs, including vibrissae, of the cat**. *J Physiol* 1972, **222**:60-61.

65. Jones LM, Depireux DA, Simons DJ, Keller A: **Robust temporal coding in the trigeminal system**. *Science* 2004, **204**:1986-1989.

66. Staba RJ, Ard TD, Benison AM, Barth DS: **Intracortical pathways mediate nonlinear fast oscillation (>200 Hz) interactions within rat barrel cortex**. *J Neurophysiol* 2005, **93**:2934-2939.

67. Barth DS: **Submillisecond synchronization of fast electrical oscillations in neocortex**. *J Neurosci* 2003, **23**:2502-2510.

68. • Arabzadeh E, Zorzin E, Diamond ME: **Neuronal encoding of texture in the whisker sensory pathway**. *PLoS Biol* 2005, **3**:e17.
This study delineates the coding of textures by the temporal structure of spike trains in primary vibrissa cortex.

69. Arabzadeh E, Petersen RS, Diamond ME: **Encoding of whisker vibration by rat barrel cortex neurons: implications for texture discrimination**. *J Neurosci* 2003, **27**:9146-9154.

70. Melzer P, Champney GC, Maguire MJ, Ebner FF: **Rate code and temporal code for frequency of whisker stimulation in rat primary and secondary somatic sensory cortex**. *Exp Brain Res* 2006, **172**:370-386.

71. Szwed M, Bagdasarian K, Ahissar E: **Coding of vibrissal active touch**. *Neuron* 2003, **40**:621-630.

72. • Ferezou I, Bolea S, Petersen CCH: **Visualizing the cortical representation of whisker touch: voltage-sensitive dye imaging in freely moving mice**. *Neuron* 2006, **50**:617-629.
The authors report the first widefield functional images from an awake, head-fixed rodent.

73. Fee MS, Mitra PP, Kleinfeld D: **Central versus peripheral determinates of patterned spike activity in rat vibrissa cortex during whisking.** *J Neurophysiol* 1997, **78**:1144-1149.

74. • Crochet S, Petersen CCH: **Correlating membrane potential with behaviour using whole-cell recordings from barrel cortex of awake mice**. *Nat Neurosci* 2006, **9**:608-610.
The authors report the first comprehensive intracellular records from an awake, head-fixed rodent.

75. Castro-Alamancos MA: **Role of thalamocortical sensory suppression during arousal: focusing sensory inputs in neocortex**. *J Neurosci* 2002, **15**:9651-9655.

76. Castro-Alamancos MA: **Absence of rapid sensory adaptation in neocortex during information processing states**. *Neuron* 2004, **41**:455-464.

77. Chapin JK, Woodward DJ: **Somatic sensory transmission to the cortex during movement: gating of single cell responses to touch**. *Exp Neurol* 1982, **78**:654-669.

78. Wrobel A, Kublik E, Musial P: **Gating of the sensory activity within barrel cortex of the awake rat**. *Exp Brain Res* 1998, **123**:117-123.

79. Ganguly K, Kleinfeld D: **Goal-directed whisking behavior increases phase-locking between vibrissa movement and electrical activity in primary sensory cortex in rat**. *Proc Natl Acad Sci USA* 2004, **101**:12348-12353.

80. Ahrens KF, Levine H, Suhl H, Kleinfeld D: **Spectral mixing of rhythmic neuronal signals in sensory cortex**. *Proc Natl Acad Sci USA* 2002, **99**:15176-15181.

81. Kleinfeld D, Mehta SB: **Spectral mixing in nervous systems: experimental evidence and biologically plausible circuits**. *Prog Theor Phys Suppl* 2006, **161**:86-98.

82. Zucker E, Welker WI: **Coding of somatic sensory input by vibrissae neurons in the rat's trigeminal ganglion**. *Brain Res* 1969, **12**:134-156.

83. Woolsey TA, Van der Loos H: **The structural organization of layer IV in the somatosensory region (SI) of mouse cerebral cortex. The description of a cortical field composed of discrete cytoarchitectonic units.** *Brain Res* 1970, **17**:205-242.

84. Derdikman D, Yu C, Haidarliu S, Bagdasarian K, Arieli A, Ahissar E: **Layer-specific touch-dependent depression and facilitation in the somatosensory cortex during artificial active whisking.** *J Neurosci* 2006. In press.

85. Bernardo KL, McCasland JS, Woolsey TA, Strominger RN: **Local intra-and interlaminar connections in mouse barrel cortex.** *J Comp Neurol* 1990, **291**:231-255.

86. Krupa DJ, Wiest MC, Shuler MG, Laubach M, Nicolelis MA: **Layer-specific somatosensory cortical activation during active tactile discrimination.** *Science* 2004, **304**:1989-1992.

87. Johnson MJ, Alloway KD: **Cross-correlation analysis reveals laminar differences in thalamocortical interactions in the somatosensory system.** *J Neurophysiol* 1996, **75**:1444-1457.

88. Ahissar E, Sosnik R, Bagdasarian K, Haidarliu S: **Temporal frequency of whisker movement. II. laminar organization of cortical representations.** *J Neurophysiol* 2001, **86**:354-367.

89. Ego-Stengel V, Souza TME, Jacob V, Shulz DE: **Spatiotemporal characteristics of neuronal sensory integration in the barrel cortex of the rat.** *J Neurophysiol* 2005, **93**:1450-1467.

90. Staiger JF, Flagmeyer I, Schubert D, Zilles K, Kotter R, Luhmann HJ: **Functional diversity of layer IV spiny neurons in rat somatosensory cortex: quantitative morphology of electrophysiologically characterized and biocytin labeled cells.** *Cereb Cortex* 2004, **14**:690-701.

91. • Schubert D, Kotter R, Luhmann HJ, Staiger JF, Morphology: **electrophysiology and functional input connectivity of pyramidal neurons characterizes a genuine layer Va in the primary somatosensory cortex.** *Cereb Cortex* 2006, **16**:223-236.
In this study the authors show that the connectivity of paralemniscal layer 5a neurons differs significantly from those of their lemniscal neighbors, layers 4 and 5b, and that a predominant aspect of layer 5a connectivity is intralaminar integration.

92. • Shepherd GM, Stepanyants A, Bureau I, Chklovskii D, Svoboda K: **Geometric and functional organization of cortical circuits.** *Nat Neurosci* 2005, **8**:782-790.
This study characterizes integration in layer 2/3 of inputs from layers 4 and 5a. By comparing functional and geometric organization, the study shows that layer 4 inputs are more numerous but individual layer 5a inputs are stronger. Further connectivity varies horizontally, that is, barrels versus septa, and by lamina.

93. Webber RM, Stanley GB: **Transient and steady-state dynamics of cortical adaptation.** *J Neurophysiol* 2006, **95**:2923-2932.

94. Boloori AR, Stanley GB: **The dynamics of spatiotemporal response integration in the somatosensory cortex of the vibrissa system.** *J Neurosci* 2006, **26**:3767-3782.

95. Hipp J, Arabzadeh E, Zorzin E, Conradt J, Kayser C, Diamond ME, Konig P: **Texture signals in whisker vibrations.** *J Neurophysiol* 2006, **95**:1792-1799.

96. Neimark MA, Andermann ML, Hopfield JJ, Moore CI: **Vibrissa resonance as a transduction mechanism for tactile encoding.** *J Neurosci* 2003, **23**:6499-6509.

97. Hartmann MJ, Johnson NJ, Towal RB, Assad C: **Mechanical characteristics of rat vibrissae: resonant frequencies and damping in isolated whiskers and in the awake behaving animal.** *J Neurosci* 2003, **23**:6510-6519.

98. Andermann ML, Ritt J, Neimark MA, Moore CI: **Neural correlates of vibrissa resonance: band-pass and somatotopic representation of high-frequency stimuli.** *Neuron* 2004, **42**:451-463.

99. Moore C, Andermann ML: **The vibrissa resonance hypothesis.** In *Neural Plasticity in Adult Somatic Sensory-Motor Systems.* Edited by Ebner FF. CRC Press; 2005:21-60.

100. Albarracin AL, Farfan FD, Felice CJ, Decima EE: **Texture discrimination and multi-unit recording in the rat vibrissal nerve.** *BMC Neurosci* 2006, **23**:e42.

101. Towal RB, Hartmann MJ: **Right-left asymmetries in the whisking behavior of rats anticipate movements.** *J Neurosci* 2006. in press.

102. Sellien H, Eshenroder DS, Ebner FF: **Comparison of bilateral whisker movement in freely exploring and head-fixed adult rats.** *Somatosens Mot Res* 2005, **22**:97-114.

103. Sachdev RN, Berg RW, Champney G, Kleinfeld D, Ebner FF: **Unilateral vibrissa contact: changes in amplitude but not timing of rhythmic whisking.** *Somatosens Mot Res* 2003, **20**:163-169.

104. Ahrens KF, Kleinfeld D: **Current flow in vibrissa motor cortex can phase-lock with exploratory whisking in rat.** *J Neurophysiol* 2004, **92**:1700-1707.

105. Gao P, Hattox AM, Jones LM, Keller A, Zeigler HP: **Whisker motor cortex ablation and whisker movement patterns.** *Somatosens Mot Res* 2003, **20**:191-198.

106. Sanderson KJ, Welker W, Shambes GM: **Reevaluation of motor cortex and of sensorimotor overlap in cerebral cortex of albino rats.** *Brain Res* 1984, **292**:251-260.

107. • Haiss F, Schwarz C: **Spatial segregation of different modes of movement control in the whisker representation of rat primary motor cortex.** *J Neurosci* 2005, **25**:1579-1587.
This work identifies a subregion of primary motor cortex the activation of which leads to rhythmic whisking in the awake animal, whereas activation of a separate, larger region leads to a shift in set point of the vibrissae.

108. Berg RW, Kleinfeld D: **Vibrissa movement elicited by rhythmic electrical microstimuation to motor cortex in the aroused rat mimics exploratory whisking.** *J Neurophysiol* 2003, **90**:2950-2963.

109. Brecht M, Sakmann B: **Whisker maps of neuronal subclasses of the rat ventral posterior medial thalamus, identified by whole-cell voltage recording and morphological reconstruction.** *J Physiol* 2002, **538**:495-515.

110. Brecht M, Schneider M, Sakmann B, Margrie T: **Whisker movements evoked by stimulation of single pyramidal cells in rat motor cortex.** *Nature* 2004, **427**:704-710.

111. • Berg RW, Friedman B, Schroeder LF, Kleinfeld D: **Activation of nucleus basalis facilitates cortical control of a brainstem motor program.** *J Neurophysiol* 2005, **94**:699-711.
This study shows that cholinergic activation of motor cortex is a necessary condition for cortical control of exploratory whisking movements.

112. Castro-Alamancos MA: **Vibrissa myoclonus driven by resonance of excitatory networks in motor cortex.** J Neurophysiol 2006. in press.

113. Cramer NP, Keller A: **Cortical control of a whisking central pattern generator.** *J Neurophysiol* 2006, **96**:209-217.

114. Deschênes M, Bourassa J, Parent A: **Striatal and cortical projections of single neurons from the central lateral thalamic nucleus in the rat.** *Neuroscience* 1996, **72**:679-687.

115. Hoffer ZS, Alloway KD: **Organization of corticostriatal projections from the vibrissal representations in the primary motor and somatosensory cortical areas of rodents.** *J Comp Neurol* 2001, **439**:87-103.

116. Lévesque M, Charara A, Gagnon S, Parent A, Deschênes M: **Corticostriatal projections from layer V cells in rat are collaterals of long-range corticofugal axons.** *Brain Res* 1996, **709**:311-315.

117. Khatri V, Hartings JA, Simons DJ: **Adaptation in thalamic barreloid and cortical barrel neurons to periodic whisker deflections varying in frequency and velocity.** *J Neurophysiol* 2004, **92**:3244-3254.

118. Engel J, Schultens HA, Schild D: **Small conductance potassium channels cause an activity-dependent spike frequency adaptation and make the transfer function of neurons logarithmic.** *Biophys J* 1999, **76**:1310-1319.

Sound Localization: cellular and local circuit influences on encoding of interaural time differences

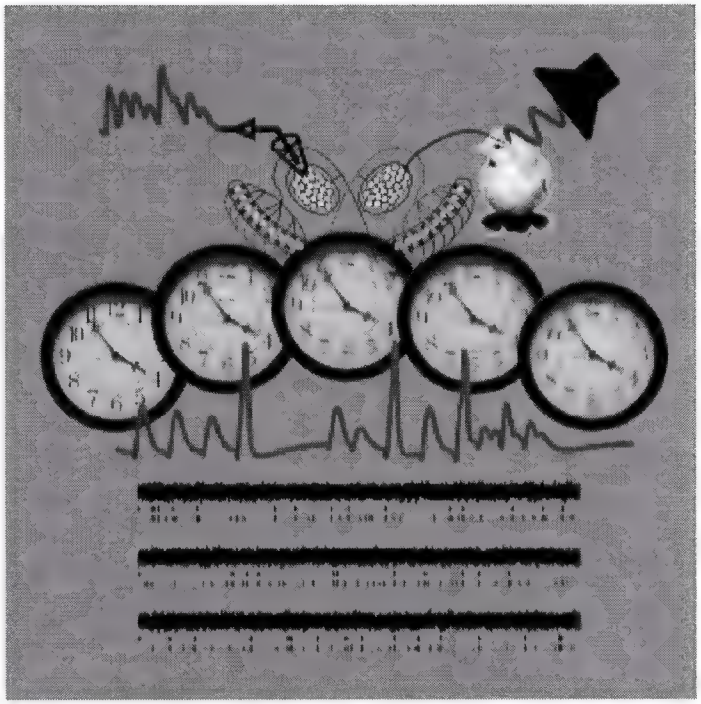
(A model system for the study of coincidence detection)

at

MCN, Woods Hole, MA, August 7, 2009

by

Bill Spain, University of Washington, Seattle



LORD RAYLEIGH
(John William Strutt)

ON OUR PERCEPTION OF SOUND DIRECTION
Philosophical Magazine, Vol. XIII. pp. 214-238, 1907

Rayleigh's predictions based on the theory of sound waves:

We might be able to detect *sound attenuation* between the two ears.

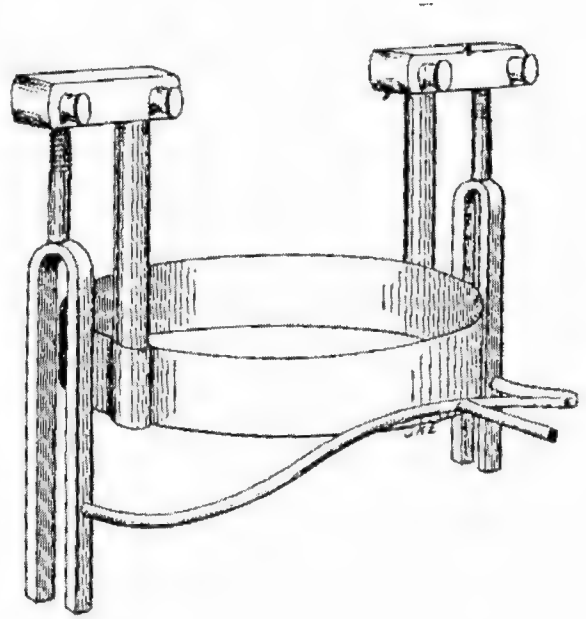
but

Attenuation of sound intensity is less for low frequency sounds because diffraction of sound is greatly reduced when the wavelength becomes longer then the size of the head*.

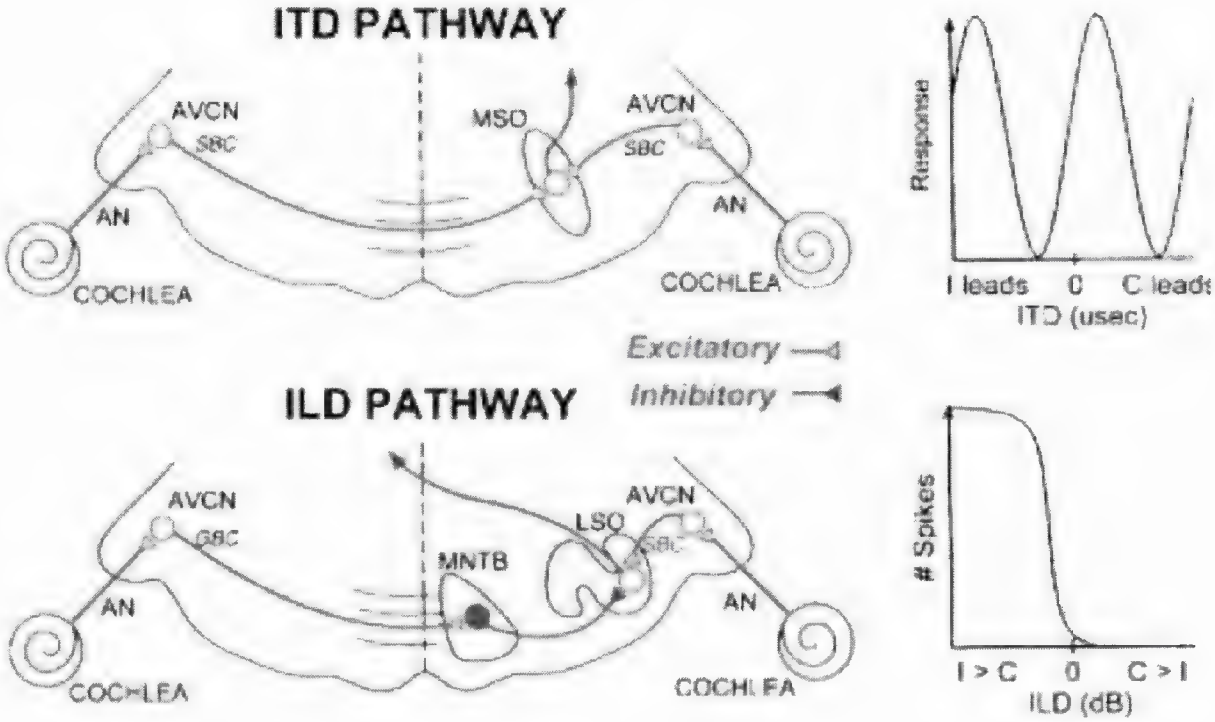
(Middle C = 261 Hz sound attenuates around the human head by ~10 % of the whole intensity)

For low frequency sound the phase difference between the two ears might be detectable. However phase ambiguity would be a problem for high frequency sounds.

Rayleigh's psychophysical experiments supported his predictions and gave birth to the *duplex theory of sound localization.*



Neural responses to ILD and ITD



from review on ILD by D.J. Tolan, Neuroscientist 2003

A Place Theory of Sound Localization

Lloyd A. Jeffress

Am. J. Psychol. 1947

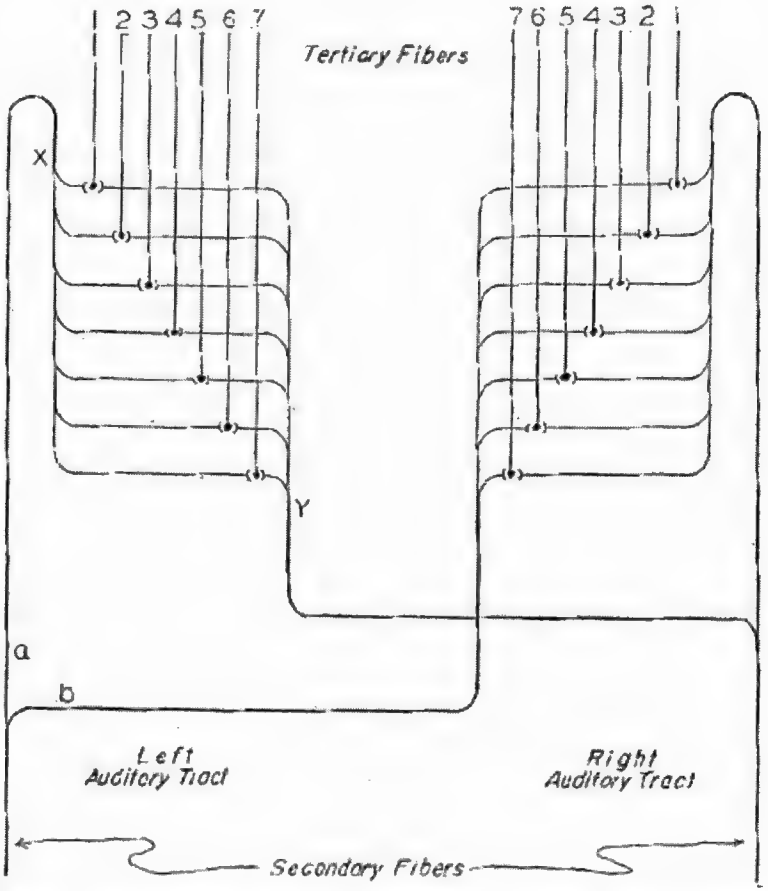
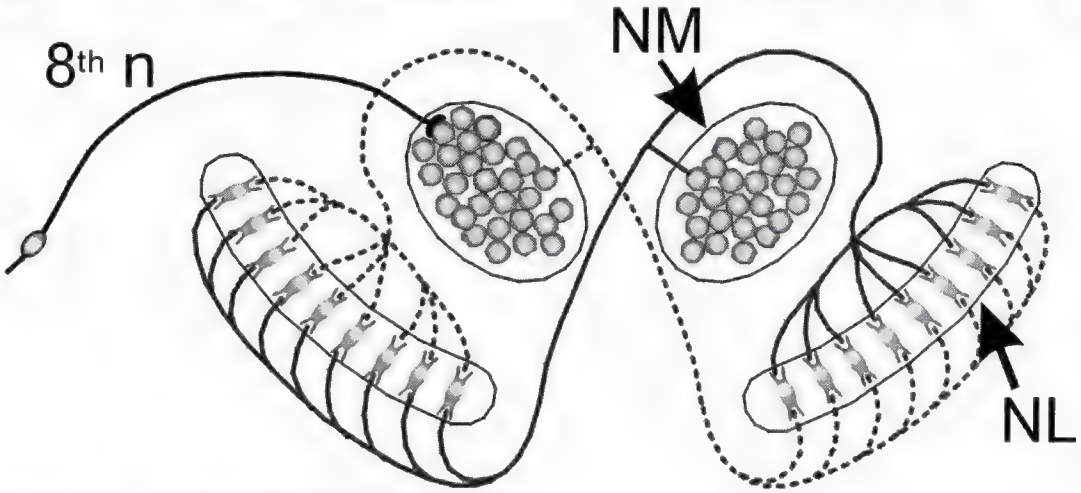


FIGURE 1. HYPOTHETICAL MID-BRAIN MECHANISM FOR THE LOCALIZATION OF LOW FREQUENCY TONES

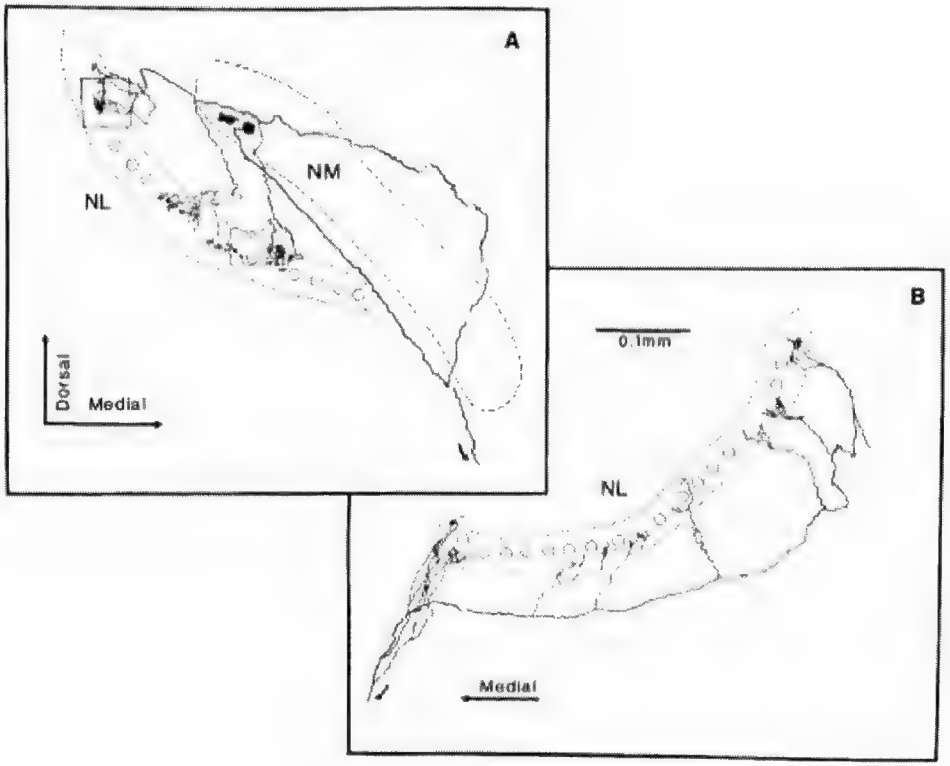
NM

NL

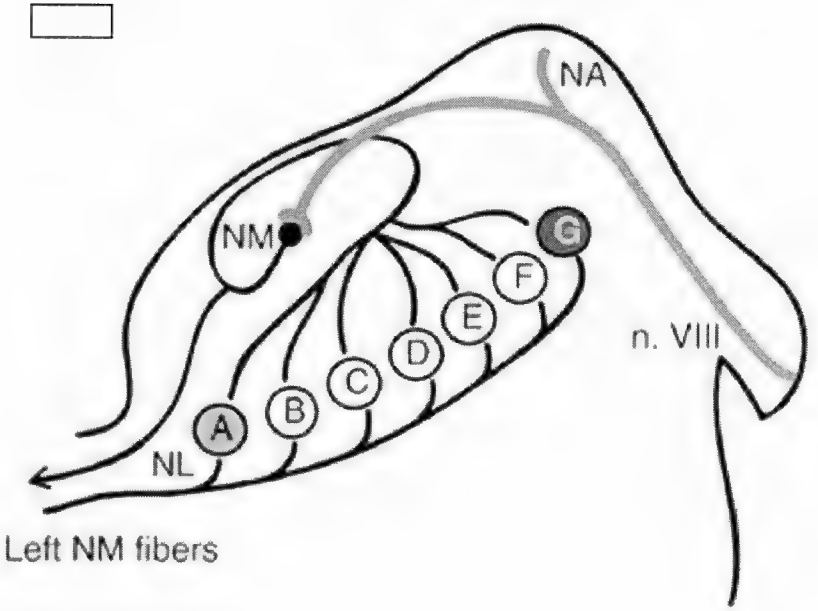


Slee et al. J. Neuroscience 2005

Evidence for Delay Lines

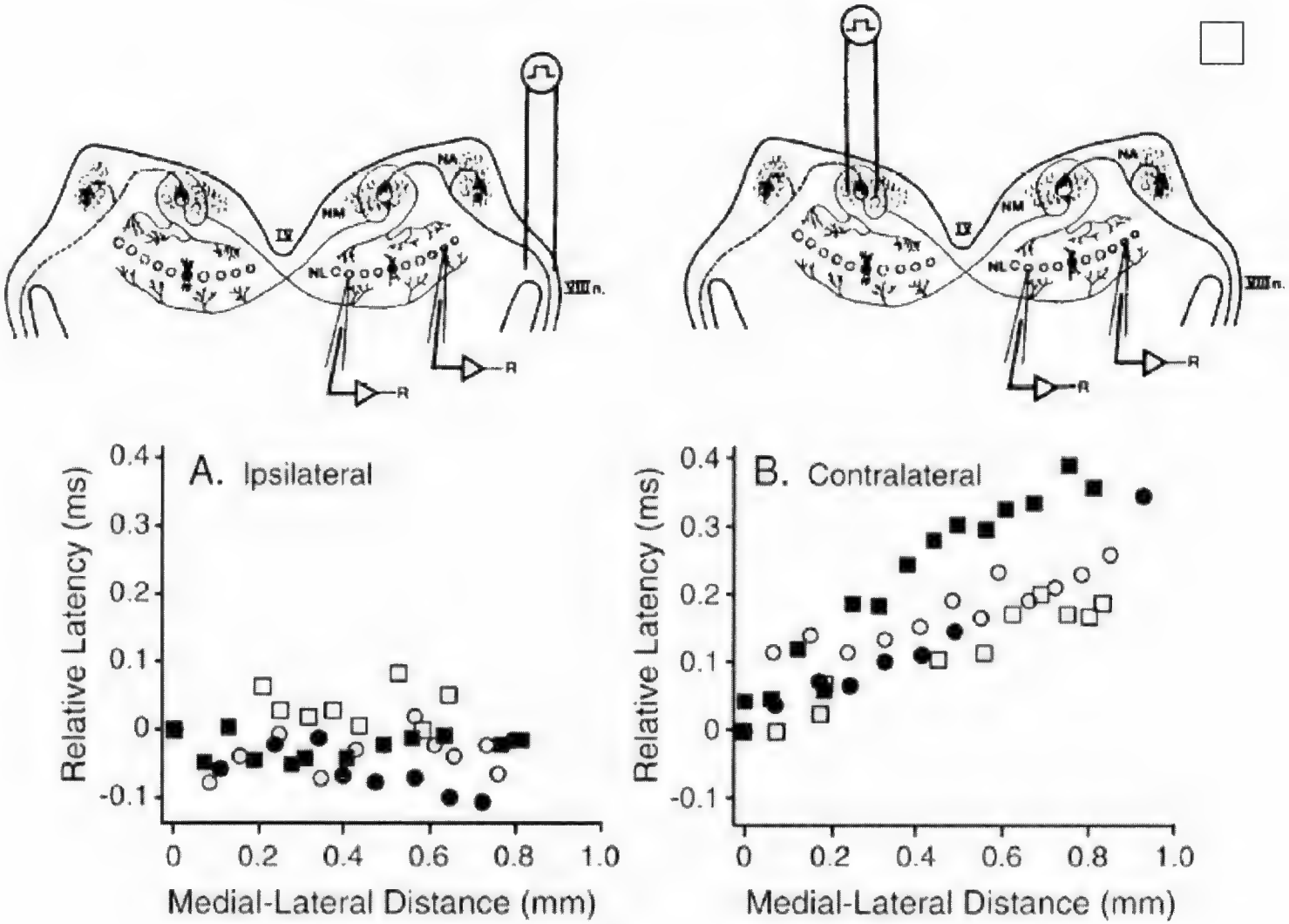


Young and Rubel J. Neurosci, 1983

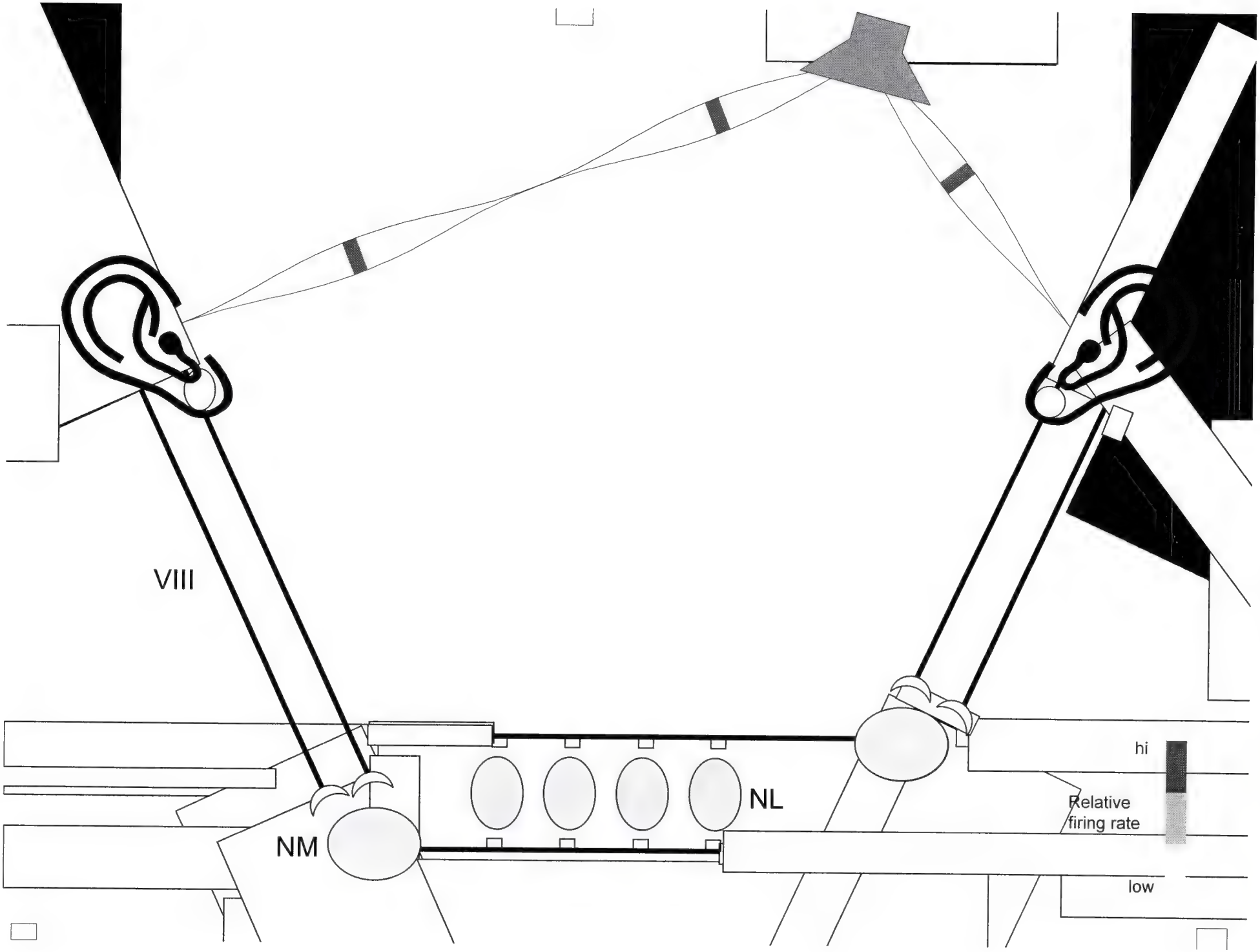


From R.L. Hyson Physiol Behav, 2005

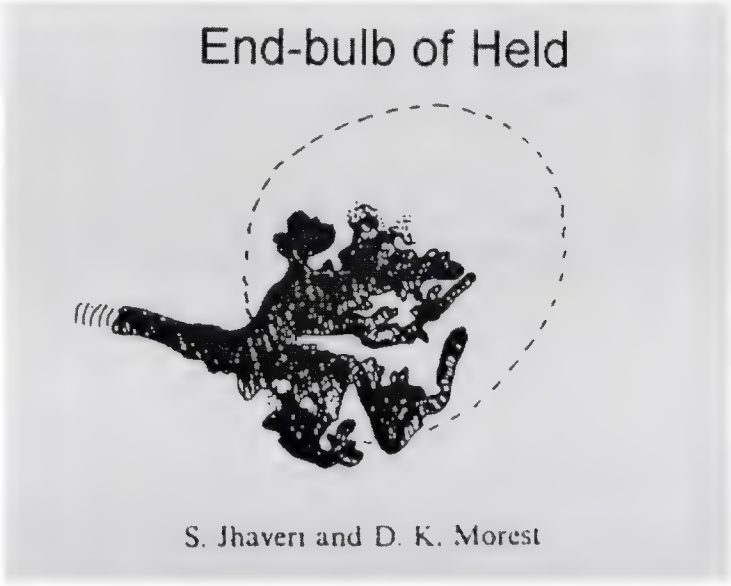
Evidence for Delay Lines

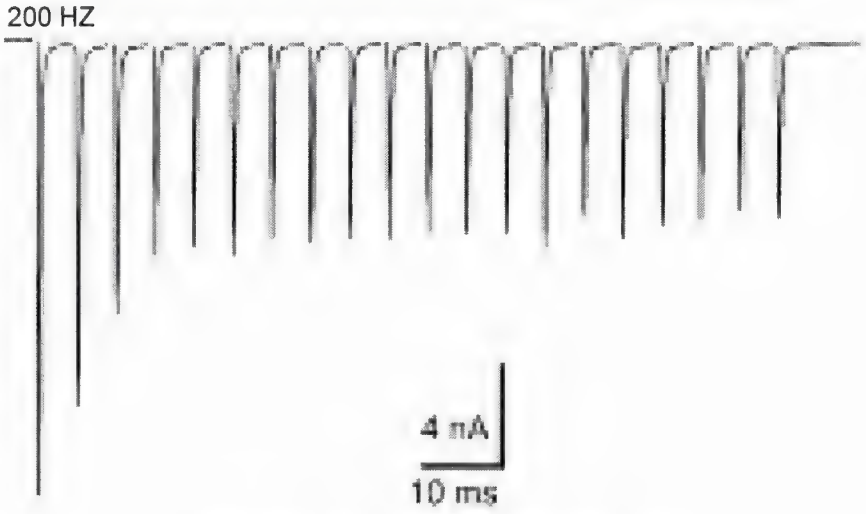


Adapted from E. M. Overholt J. Neuroscince, 1992


VIII
NM
NL
hi
Relative
firing rate
low

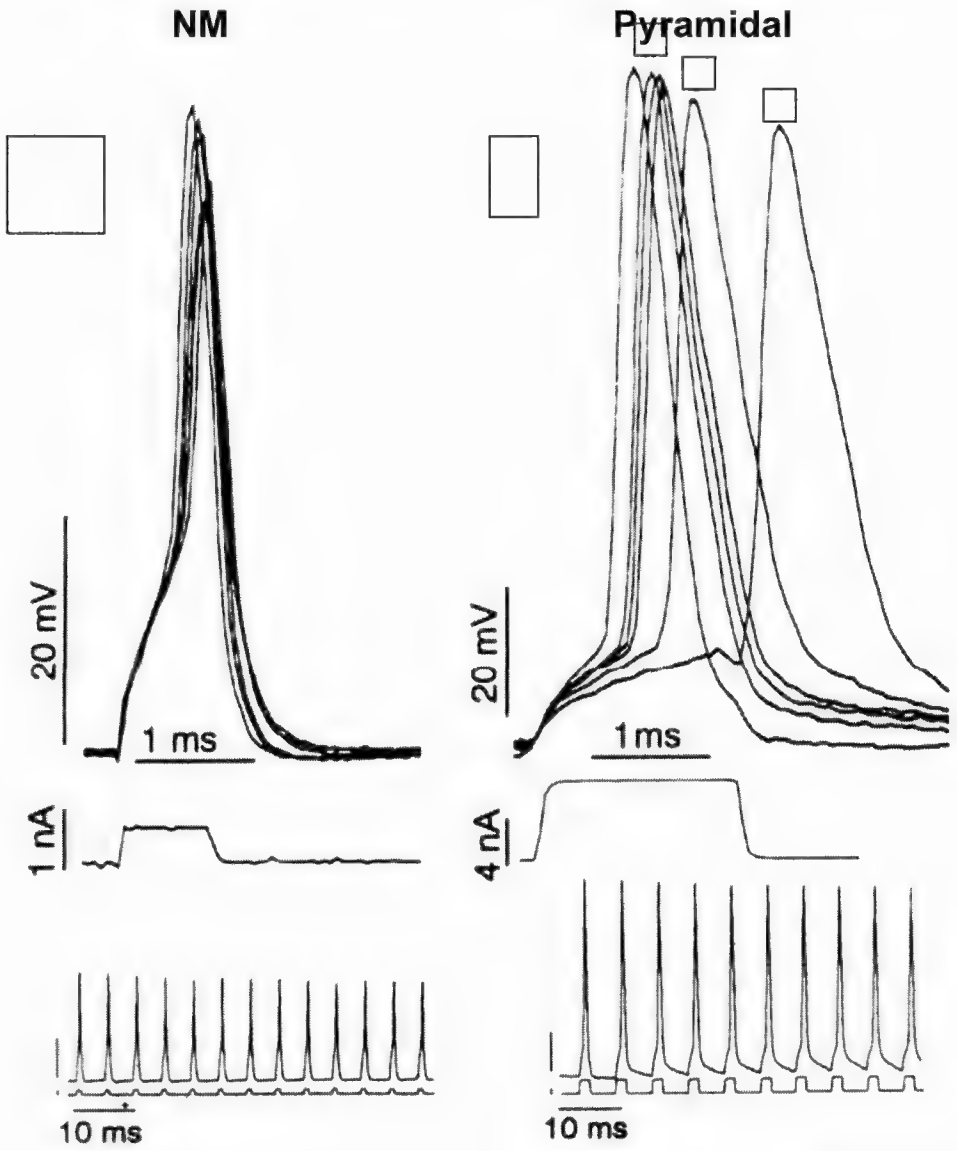
Secure and Fast Synapse





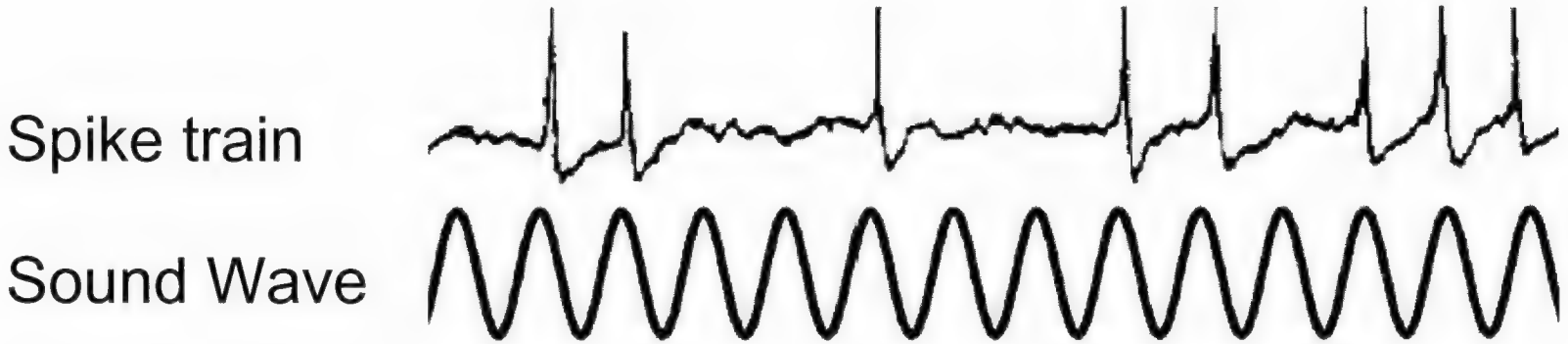
Brenowitz and Trussell J. Neurosci., 2001

Spike time precision and reproducibility

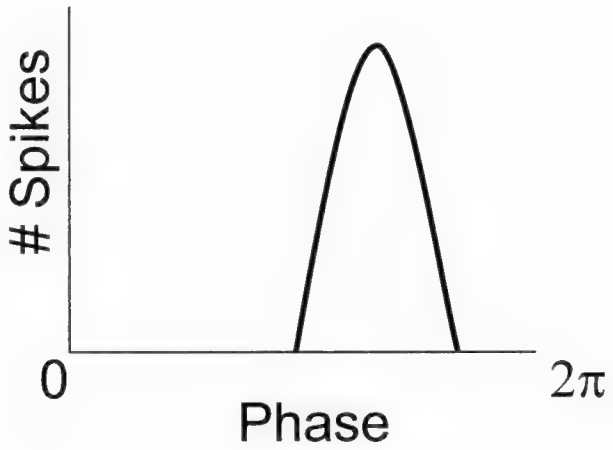


Reyes Rubel and Spain J. Neurosci, 1994

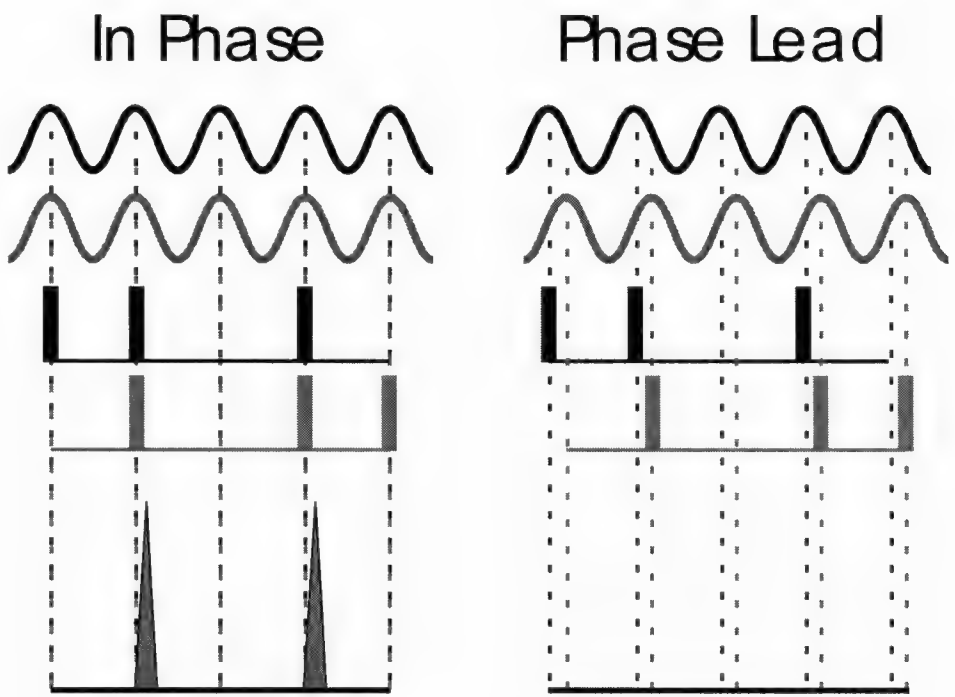
Timing information is represented in the N8, NM, and NL by **phase-locking** in response to sound.



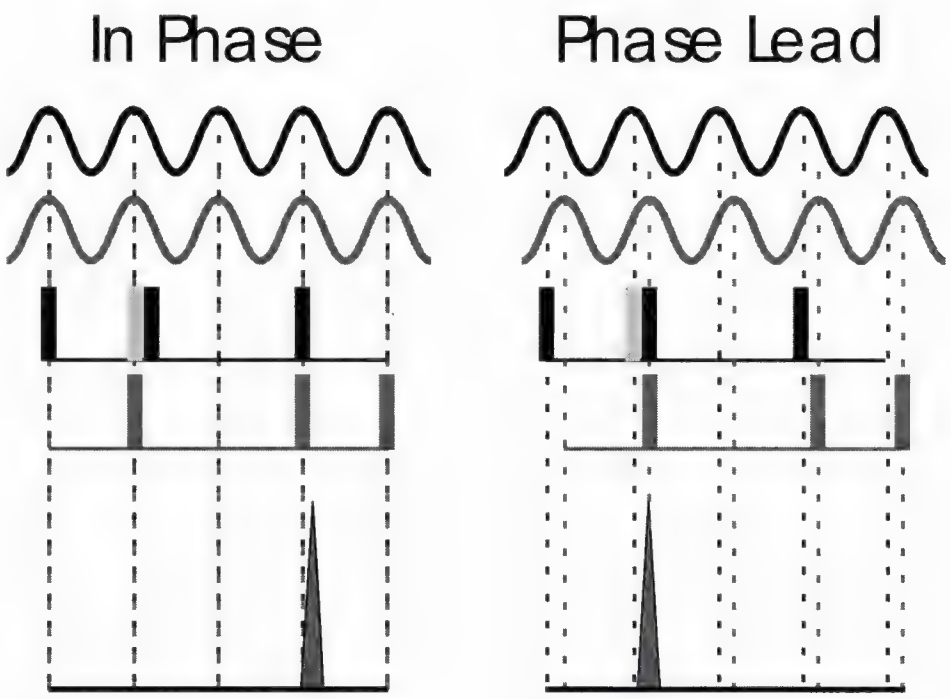
Phase-locking is represented with a **period histogram**.



Memory disrupts coincidence detection of phase-locked inputs

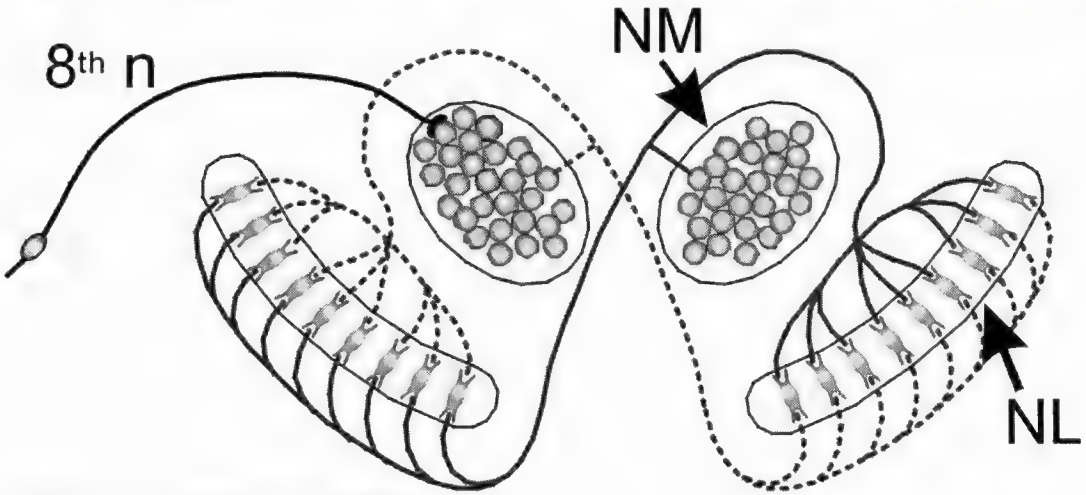


Memory disrupts coincidence detection of phase-locked inputs



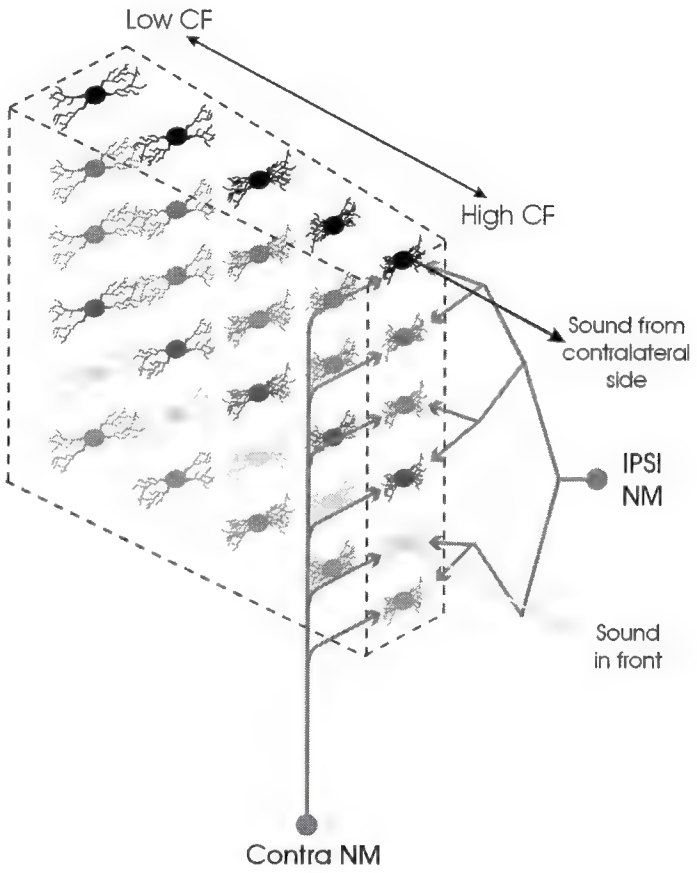
NM

NL

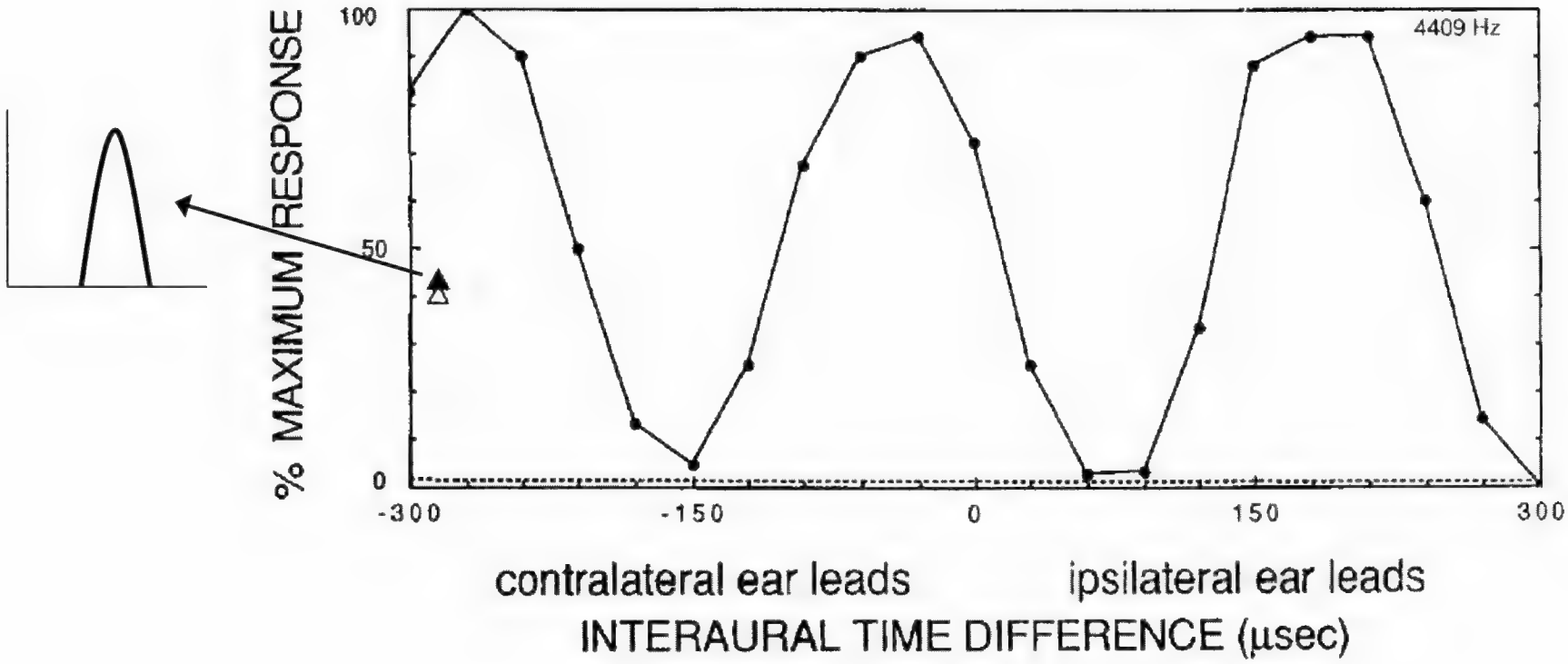


Slee et al. J. Neuroscience 2005

Organization of the place code with respect to frequency

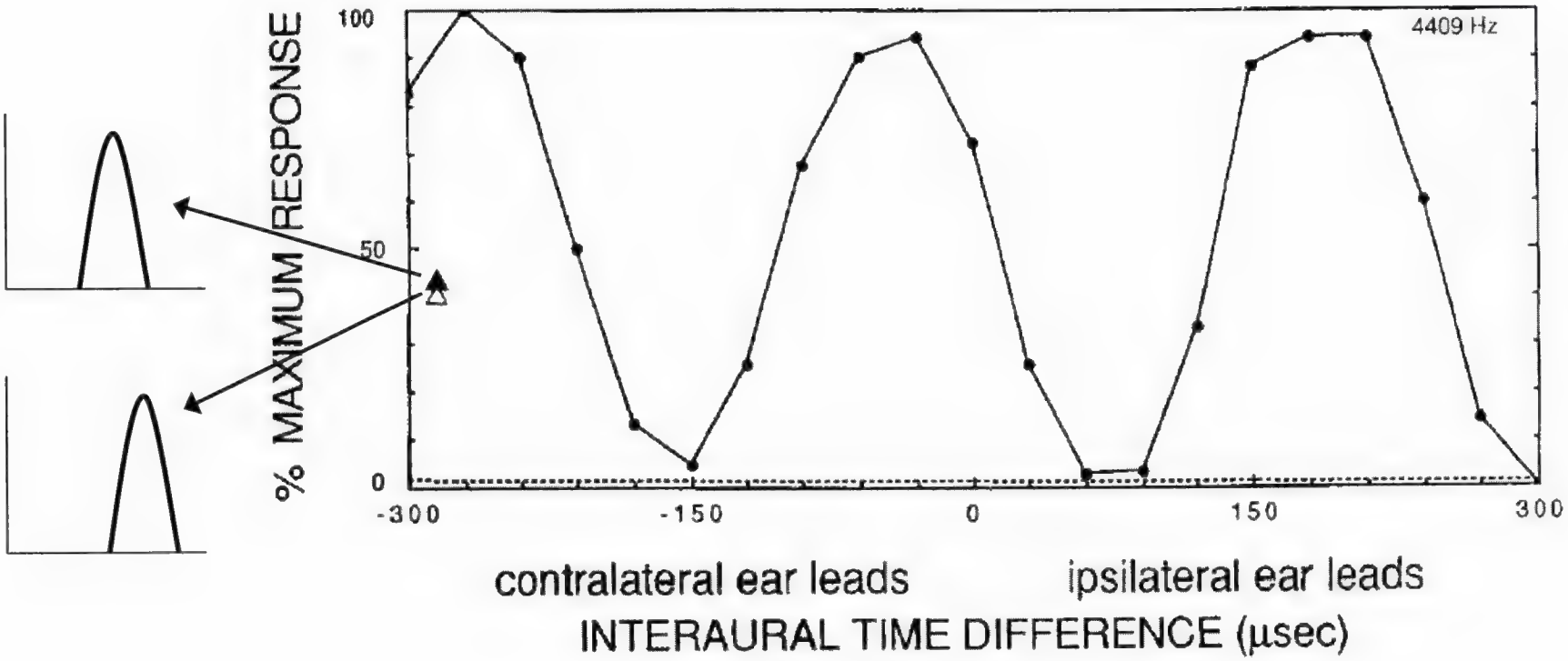


Nucleus Laminaris (NL) neurons modulate firing rate as a function of ITD



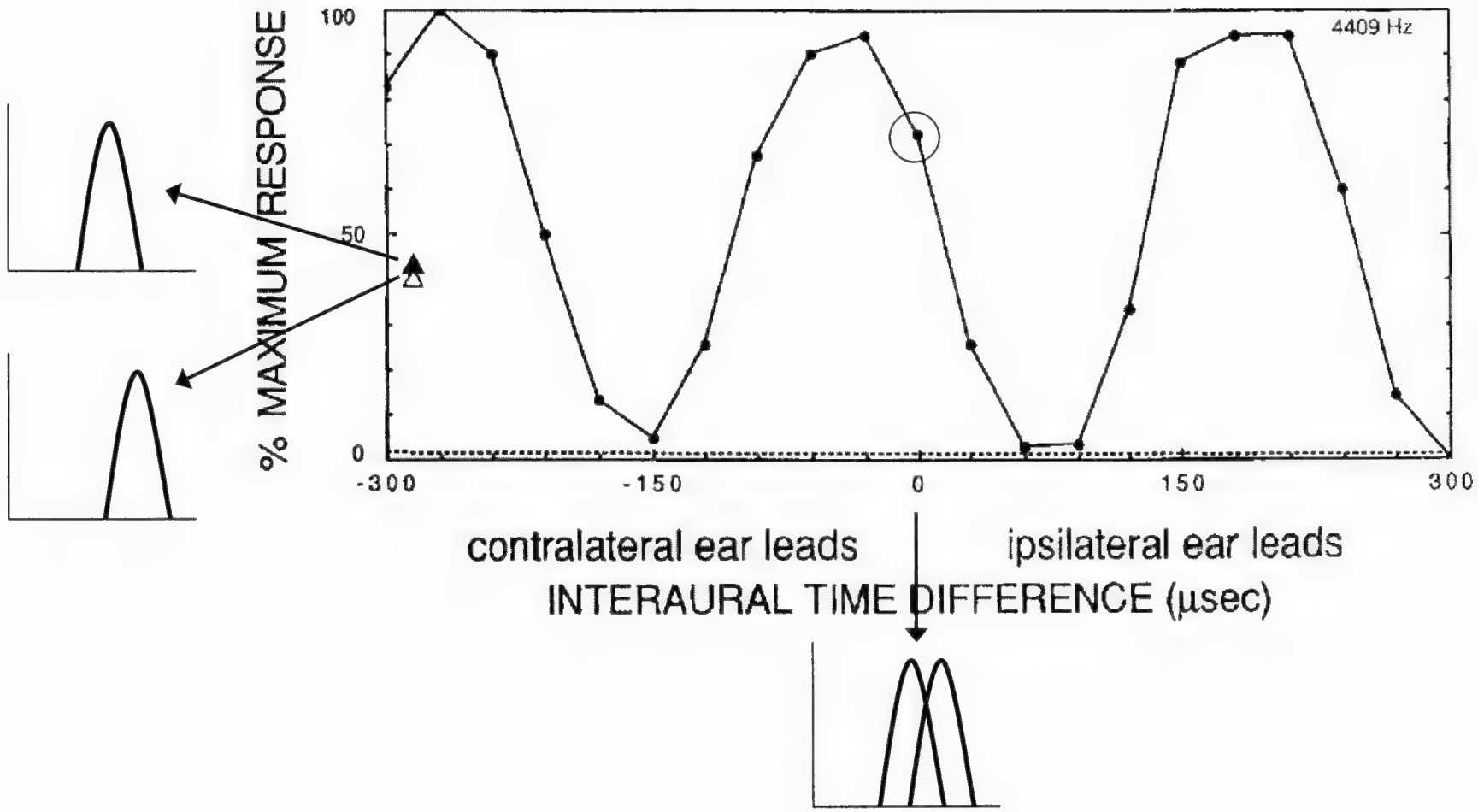
Carr and Konishi,1990

Nucleus Laminaris (NL) neurons modulate firing rate as a function of ITD



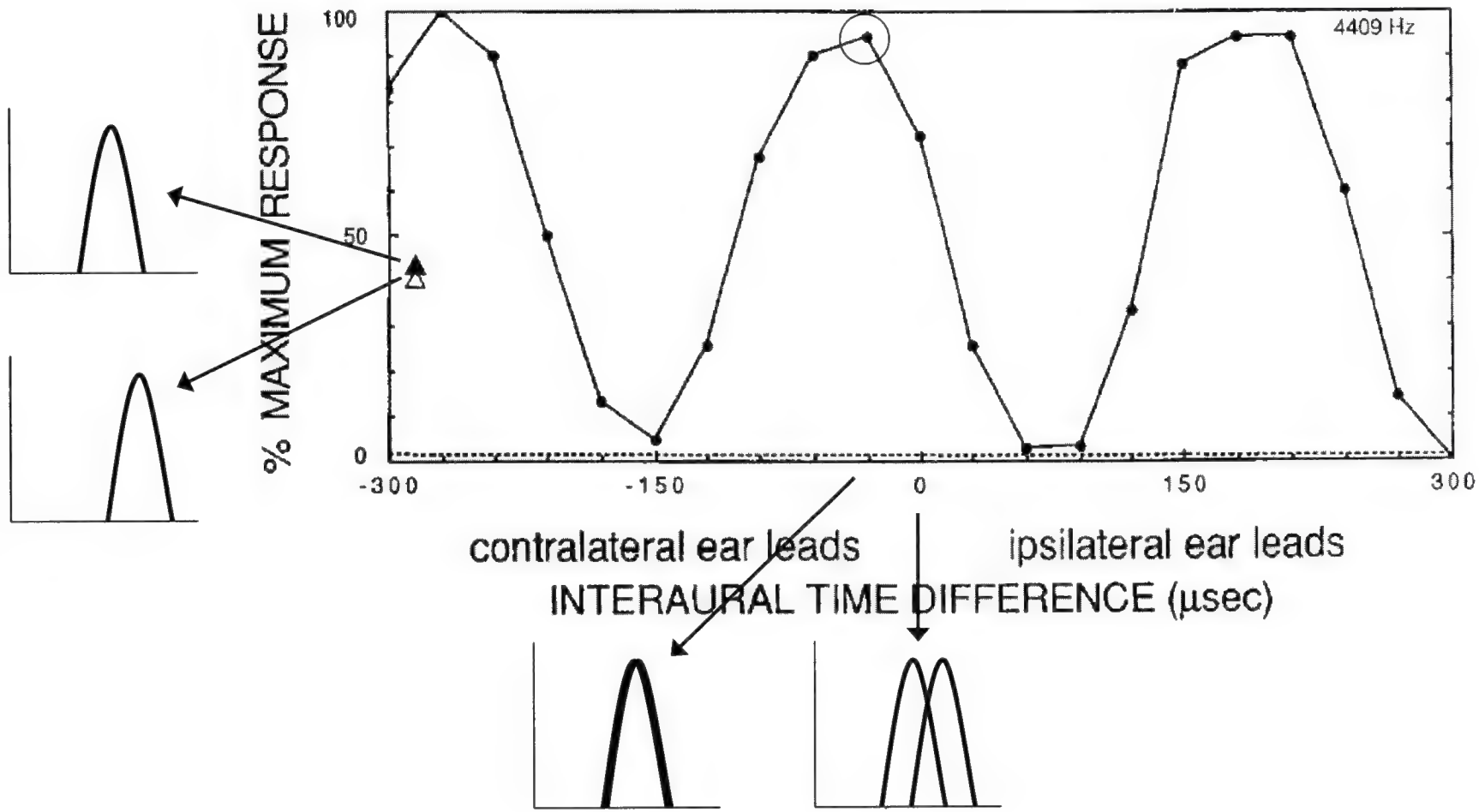
Carr and Konishi,1990

Nucleus Laminaris (NL) neurons modulate firing rate as a function of ITD



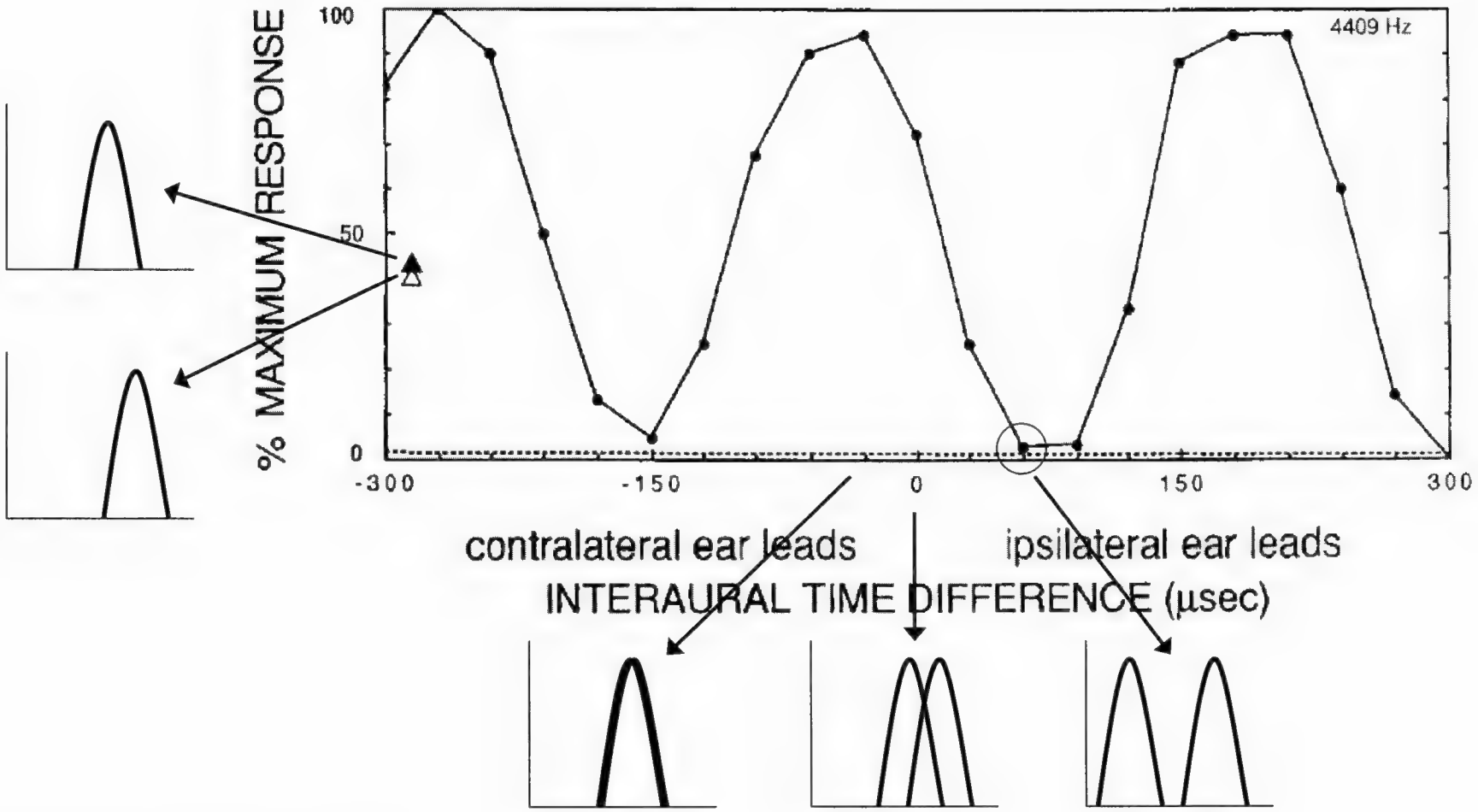
Carr and Konishi,1990

Nucleus Laminaris (NL) neurons modulate firing rate as a function of ITD



Carr and Konishi,1990

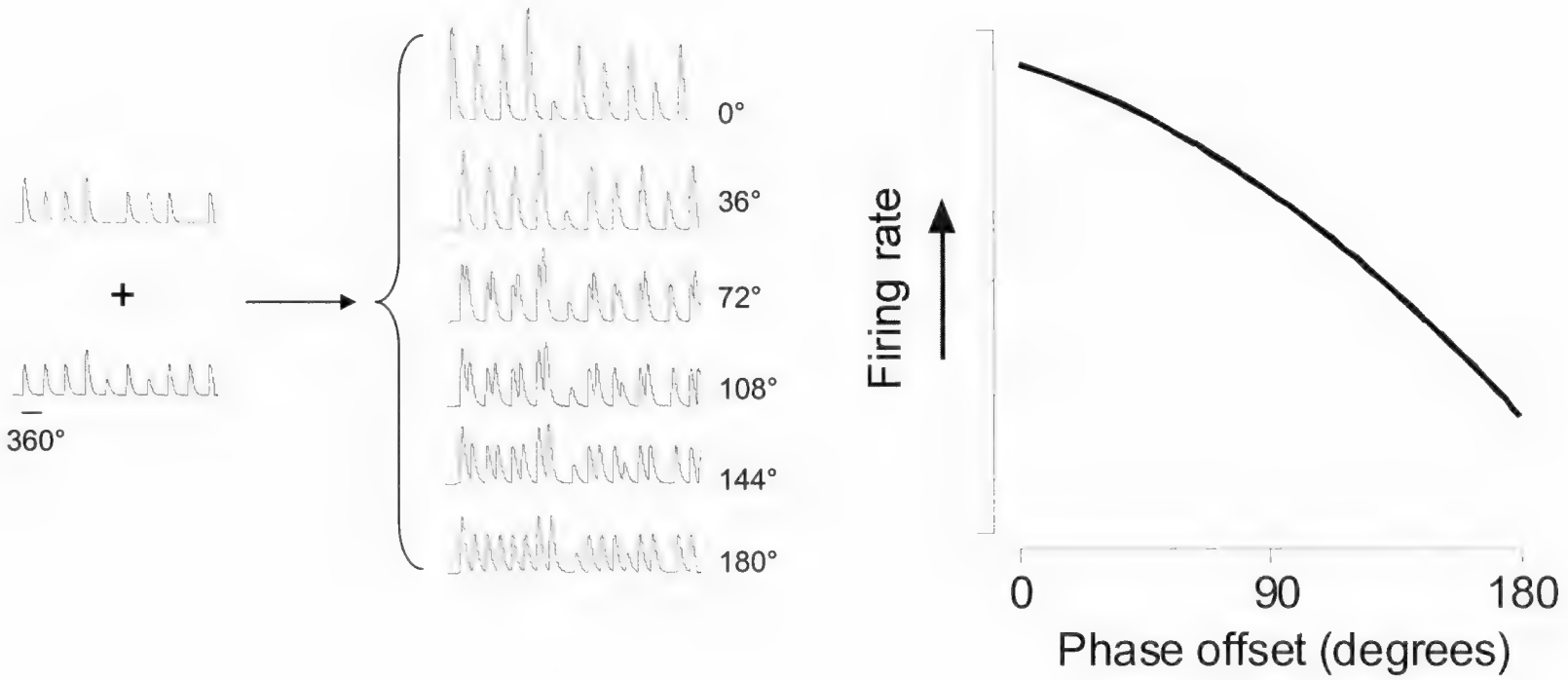
Nucleus Laminaris (NL) neurons modulate firing rate as a function of ITD



Carr and Konishi,1990

How do Neurons Perform Coincidence Detection?

Modulation of Firing Rate as a Function of Phase Delayed EPSPs is a Special Case of Selectivity for Variability of Input Amplitude

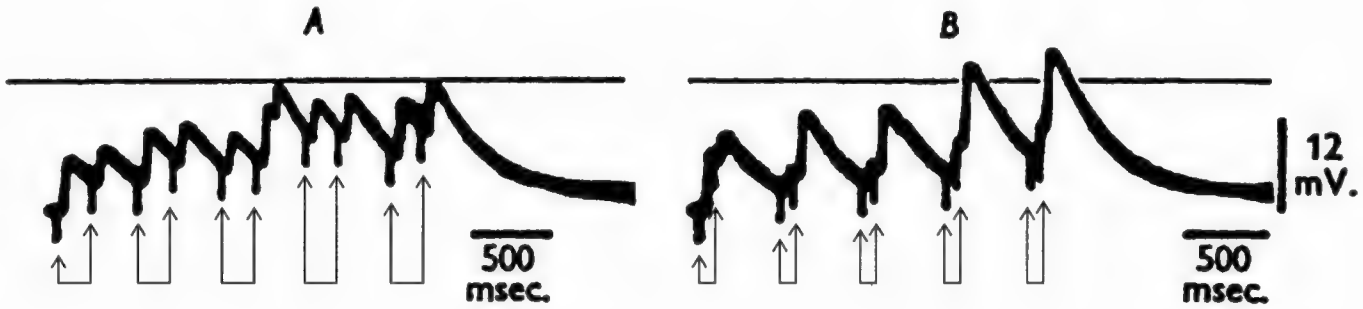


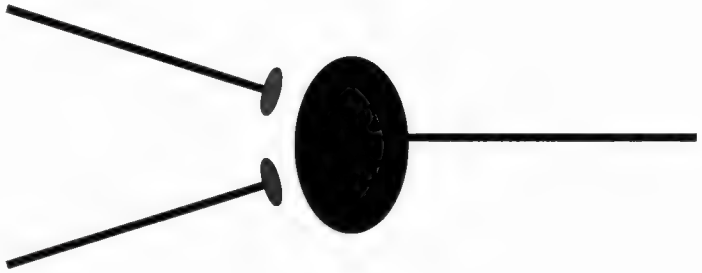
The Firing Probability Depends on the Phase Delay Between Two Inputs

From

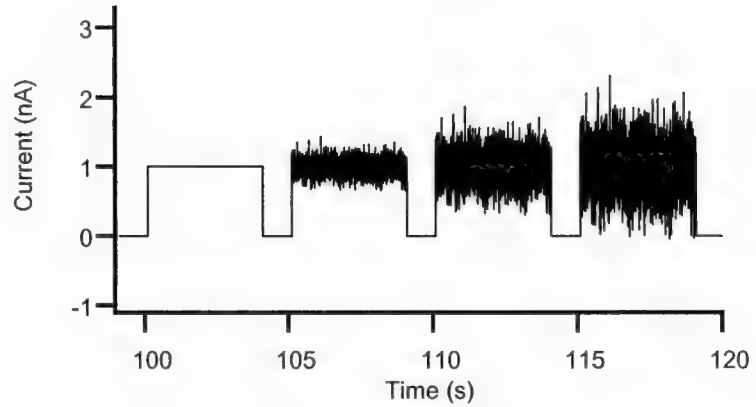
J.P. Segundo, G P. Moore, L.J. Stensaas and T.H. Bullock

Sensitivity of neurone in *Aplysia* to temporal pattern of arriving impulses. J. Exp. Biol. 40: 1963

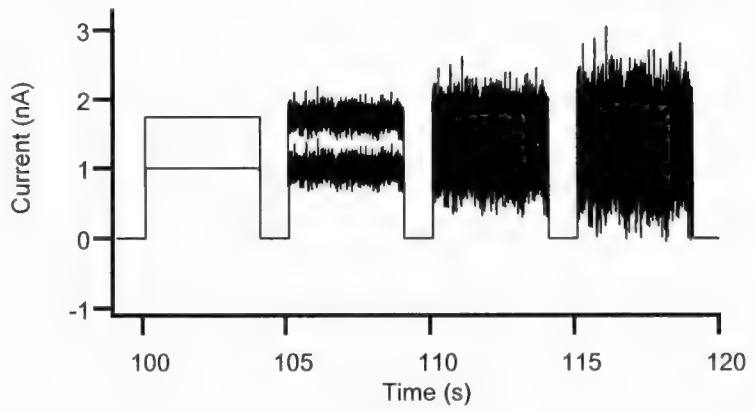




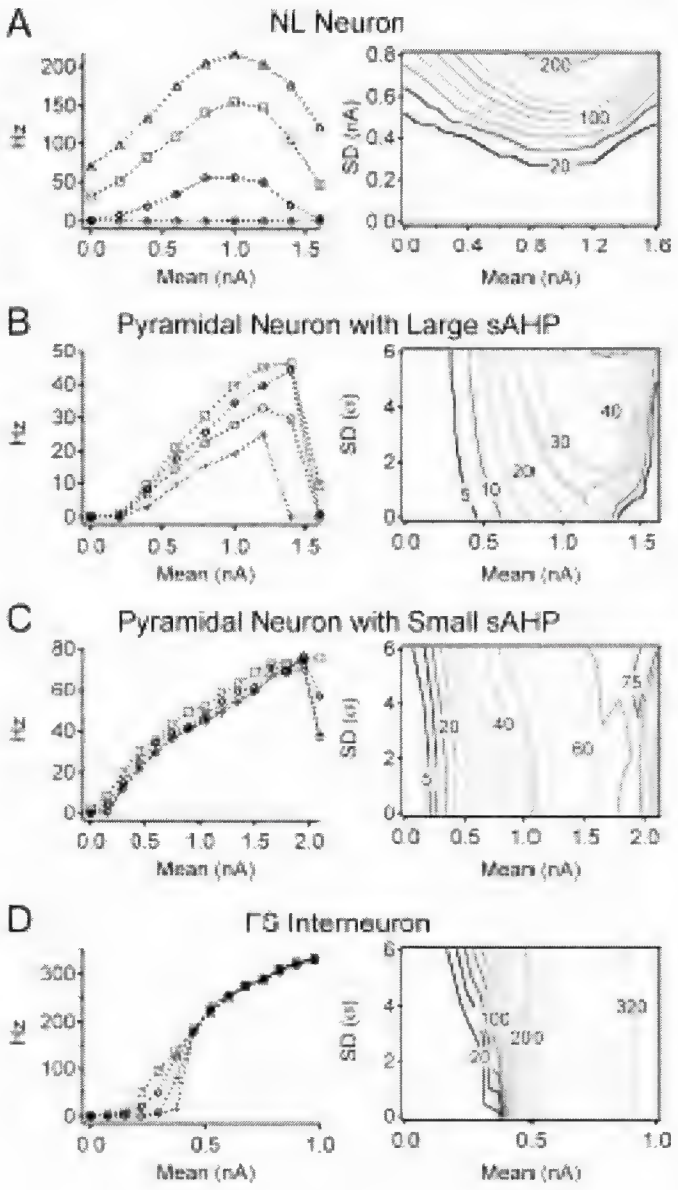
How Do Neurons Respond to DC vs. Variable Inputs?

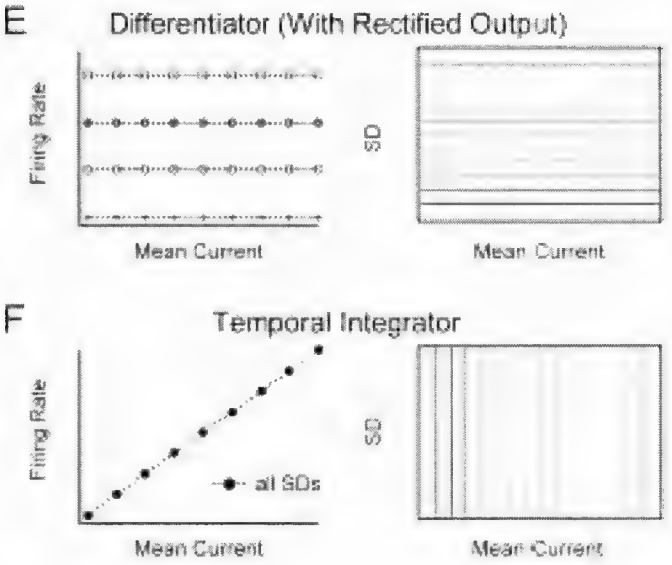


How Do Neurons Respond to DC vs. Variable Inputs?



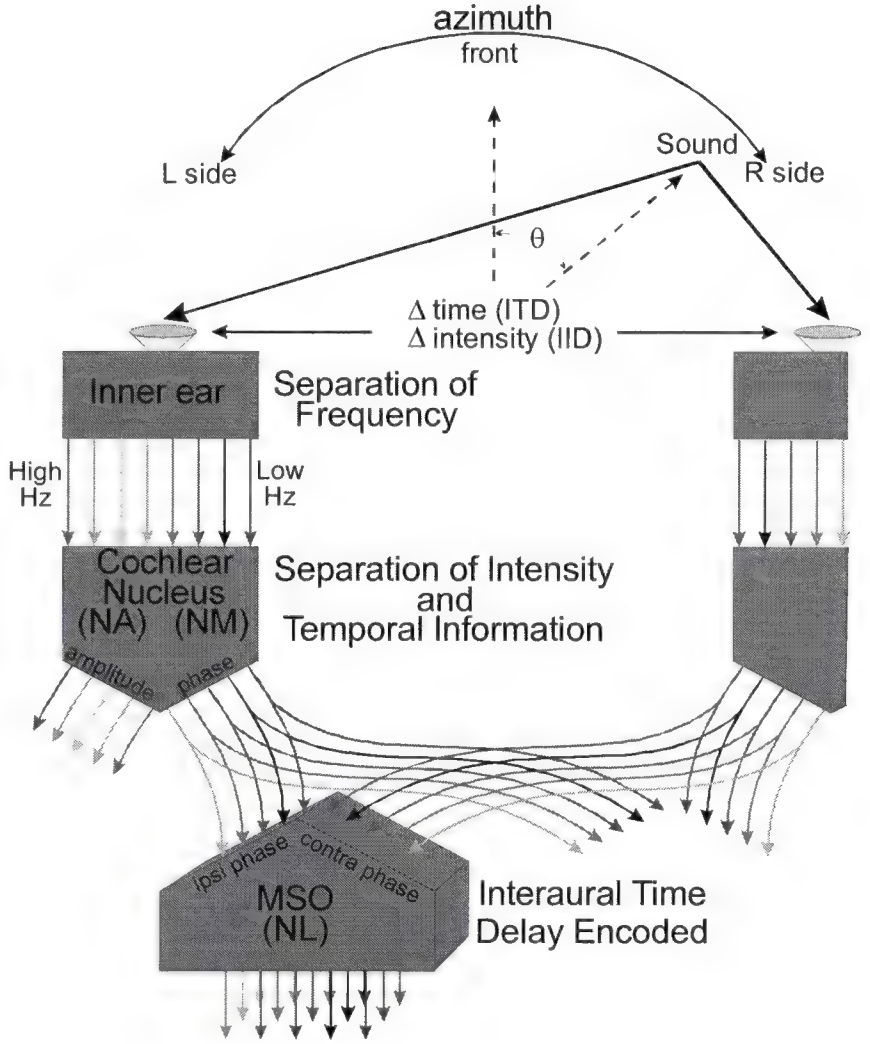
Input Selectivity in Different Types of Neurons



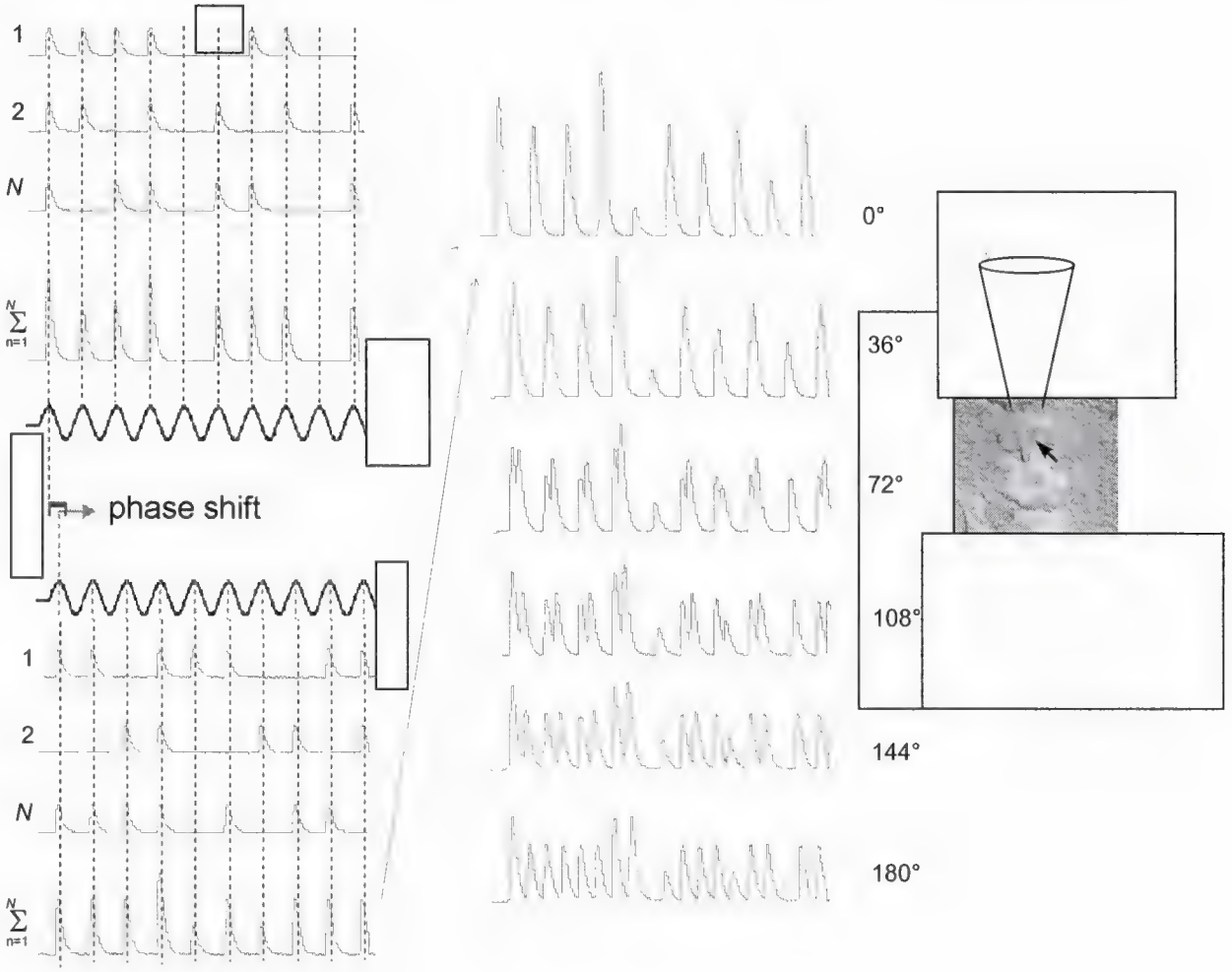


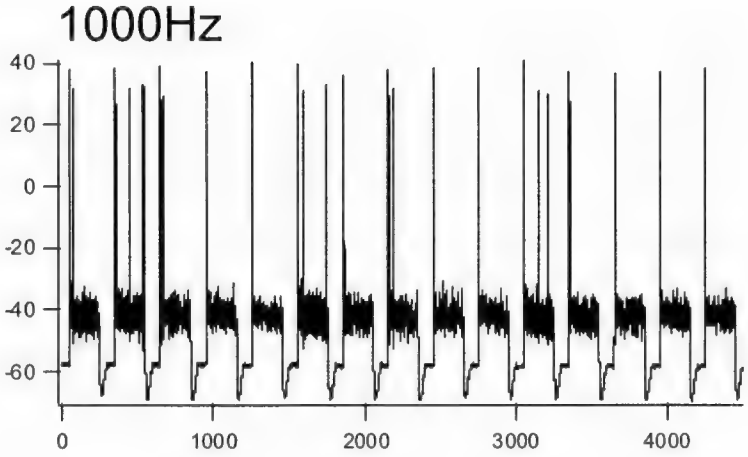
M. Higgs et al. J. Neuroscience, 2006

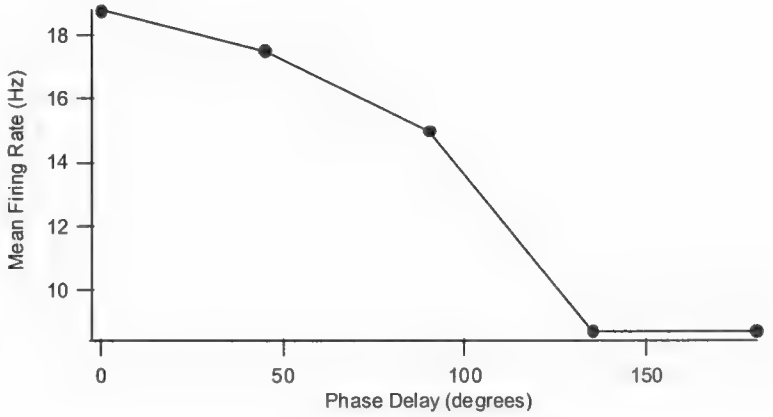
Tonotopic organization is maintained through separate ITD and ILD pathways

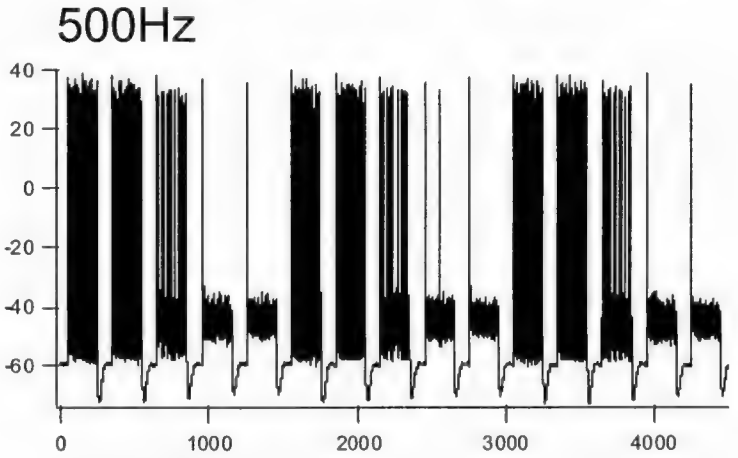


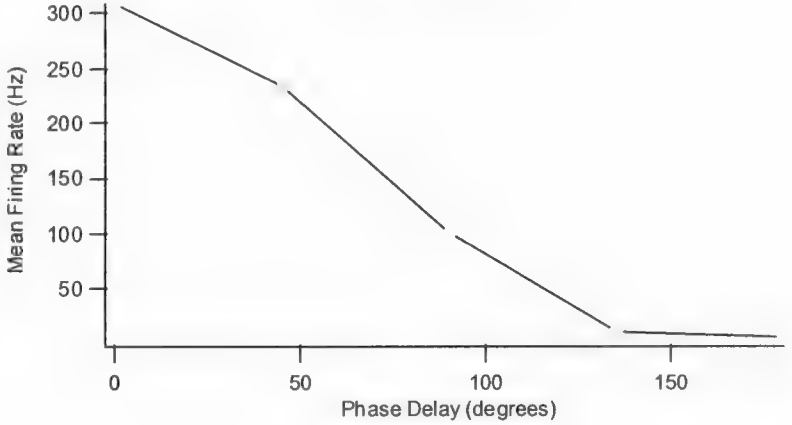
Protocol for determining the ability of NL neurons to encode "ITD" *in vitro* using simulated phase delayed EPSC trains

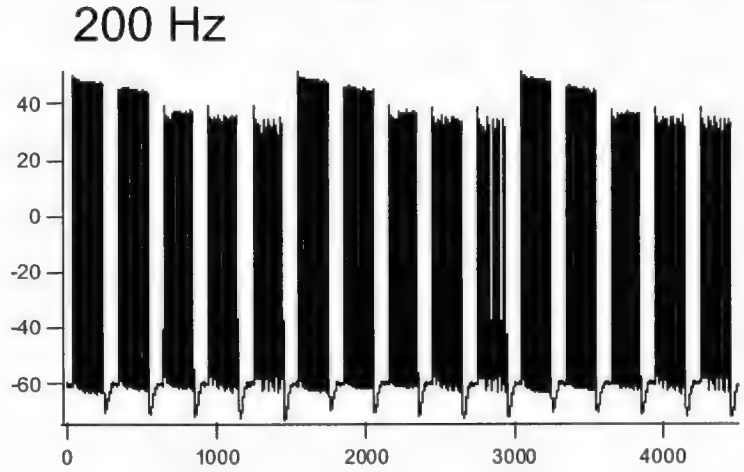


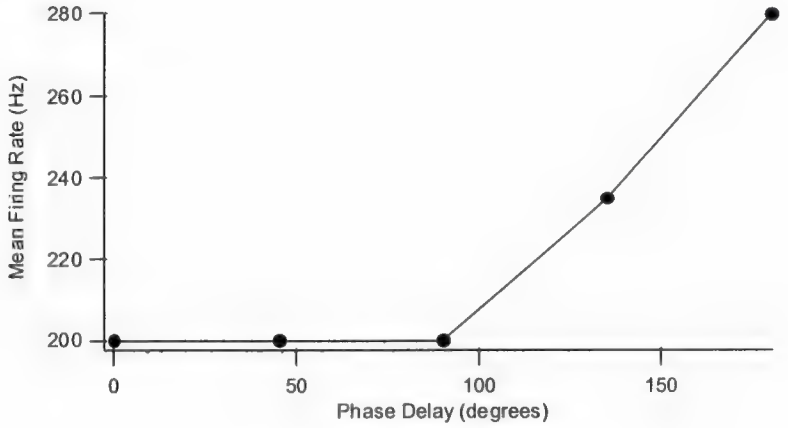

1000Hz
40
20
0
-20
-40
-60
0
1000
2000
3000
4000

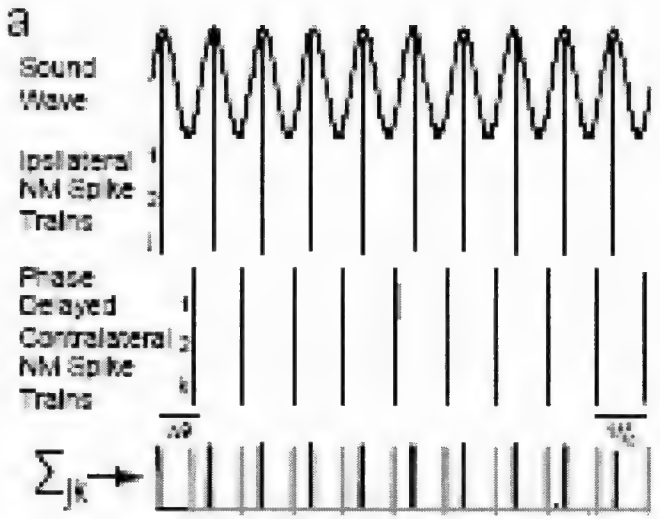

Mean Firing Rate (Hz)
18
16
14
12
10
0
50
100
150
Phase Delay (degrees)


500Hz
40
20
0
-20
-40
-60
0
1000
2000
3000
4000

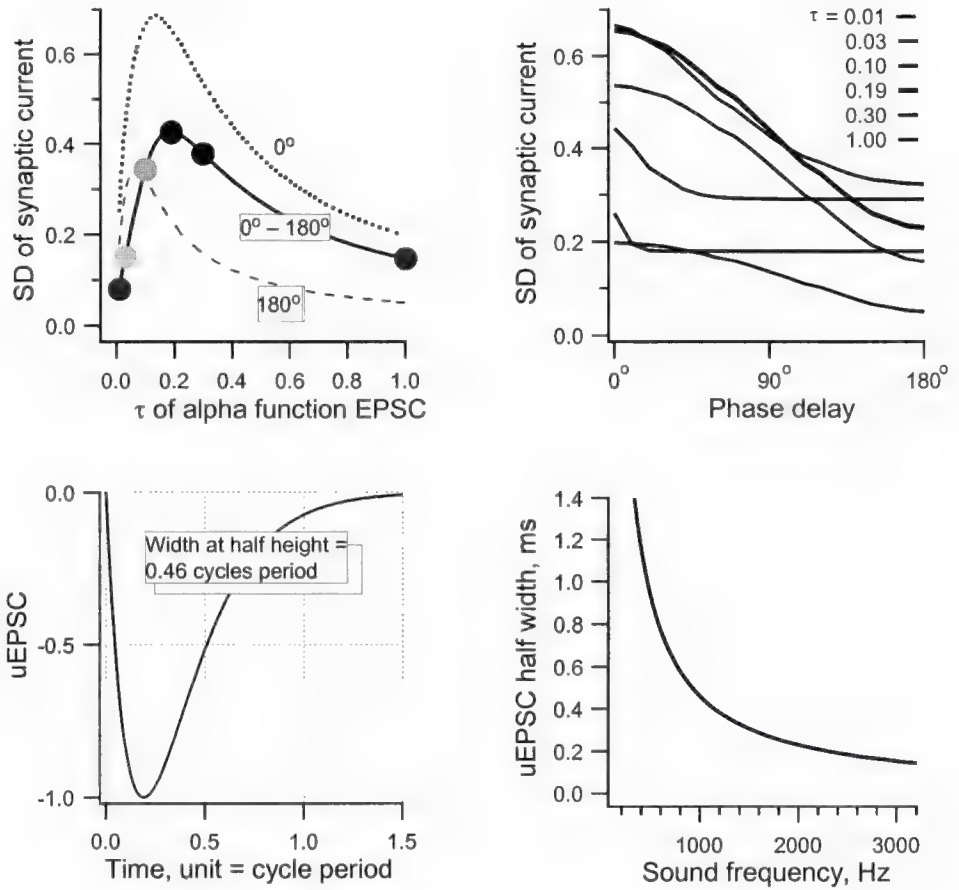

Mean Firing Rate (Hz)
300
250
200
150
100
50
0
50
100
150
Phase Delay (degrees)


200 Hz
40
20
0
-20
-40
-60
0
1000
2000
3000
4000


Mean Firing Rate (Hz)
280
260
240
220
200
0
50
100
150
Phase Delay (degrees)

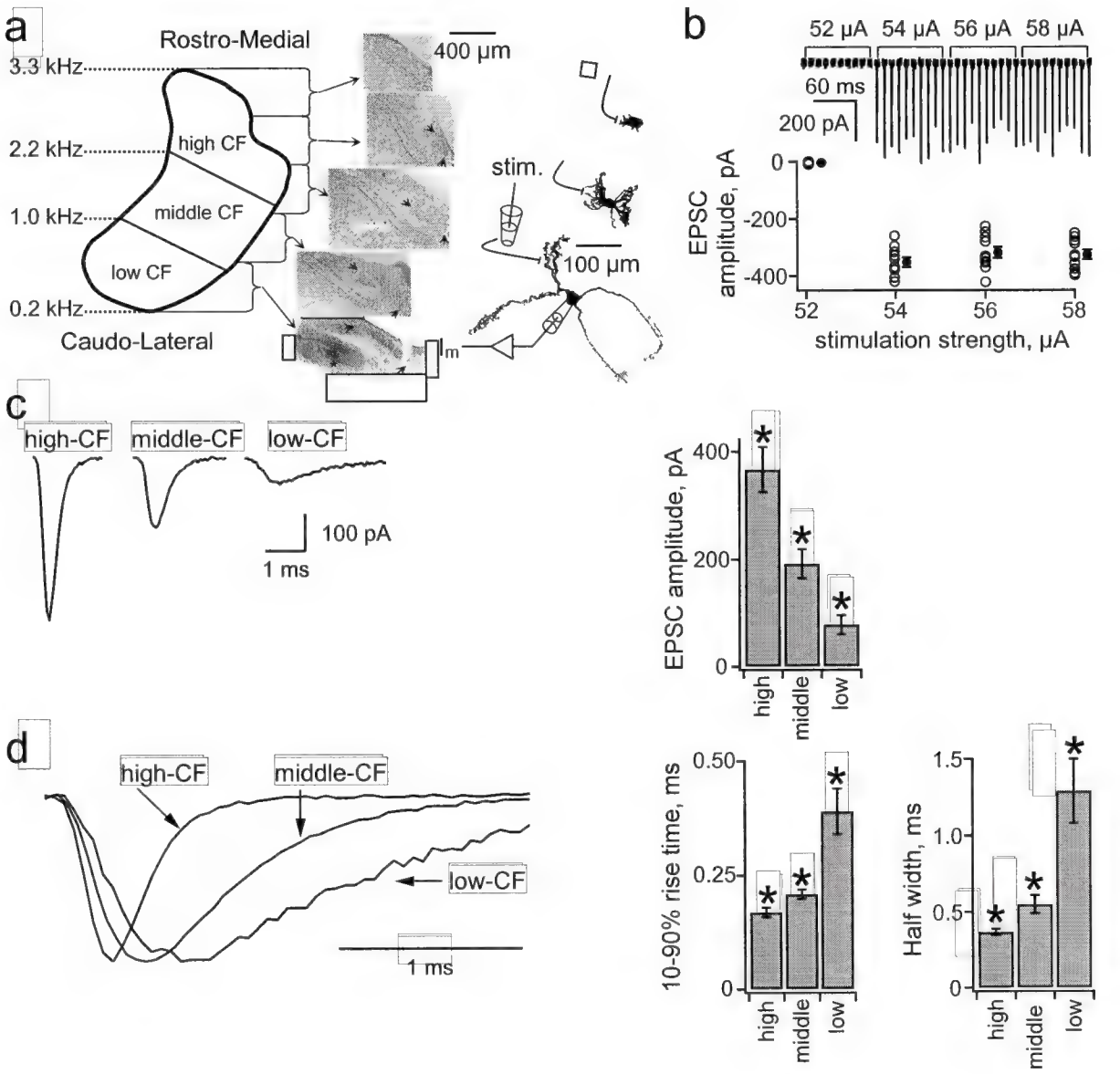

a
Sound
Wave
Ipsilateral
NM Spike
Trains
Phase
Delayed
Contralateral
NM Spike
Trains
$\sum_{jk}$

There is an optimal EPSC time-course for each tone frequency that gives the largest change of input fluctuations as IPD changes



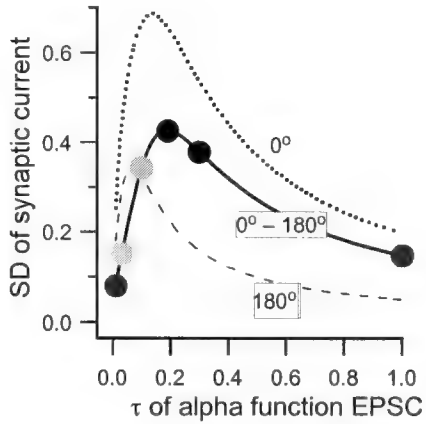
M. Higgs et al. unpublished

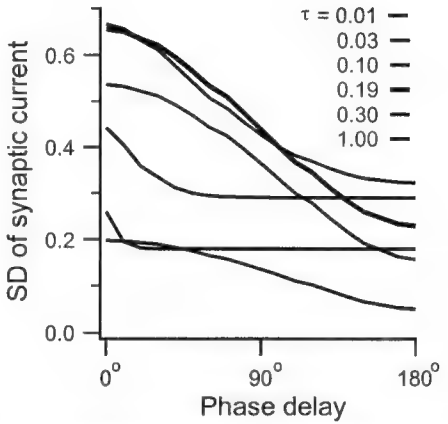
Measurement of uEPSCs of the NM to NL synapse

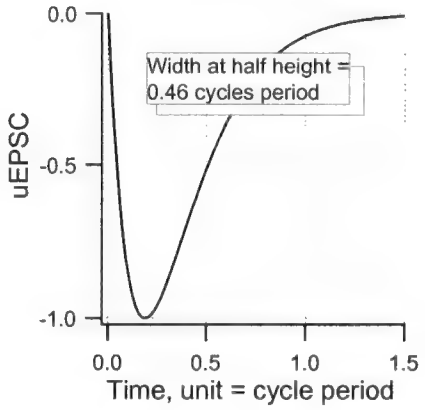


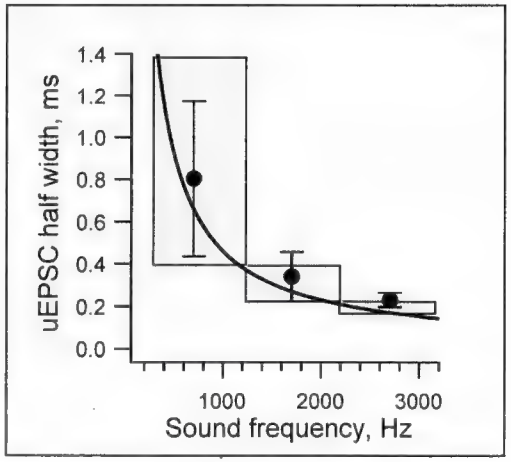
S. Slee et al. unpublished

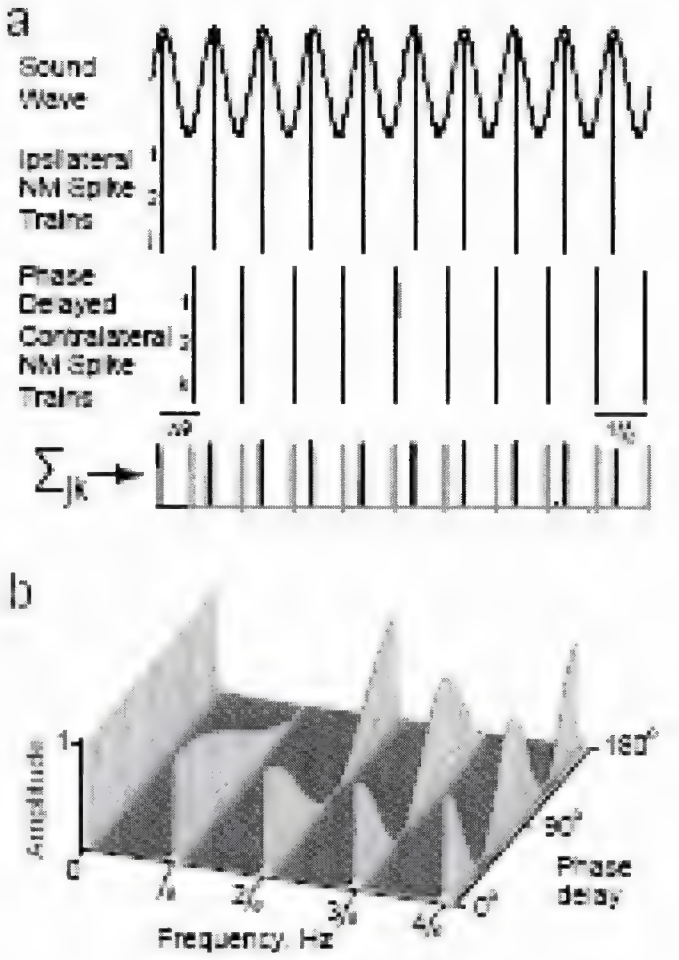
The awesome power of evolution



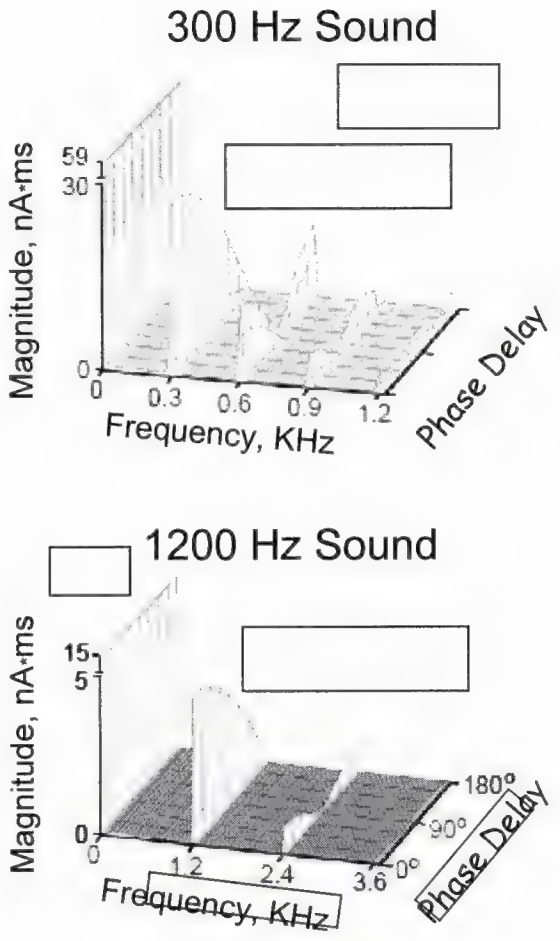




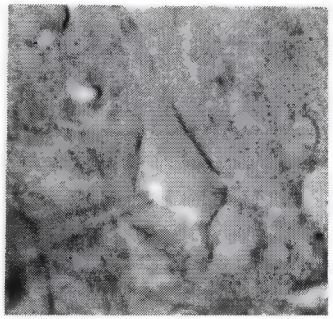



a
Sound Wave
Ipsilateral NM Spike Trains
Phase Delayed Contralateral NM Spike Trains
b
Amplitude
1
0
Frequency, Hz
180°
90°
0°
Phase delay

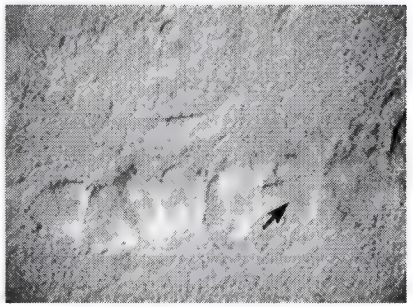
Input power decreases with phases delay *only* at the frequency of the tone



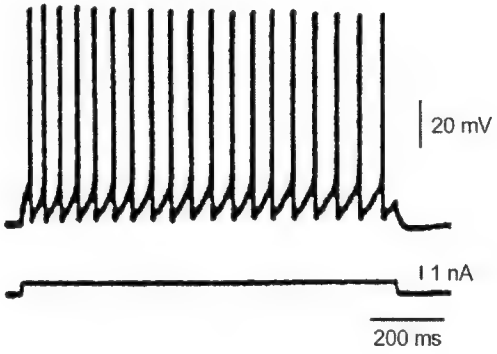
NL neurons filter the DC component of their input

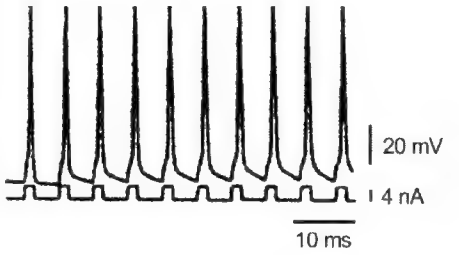


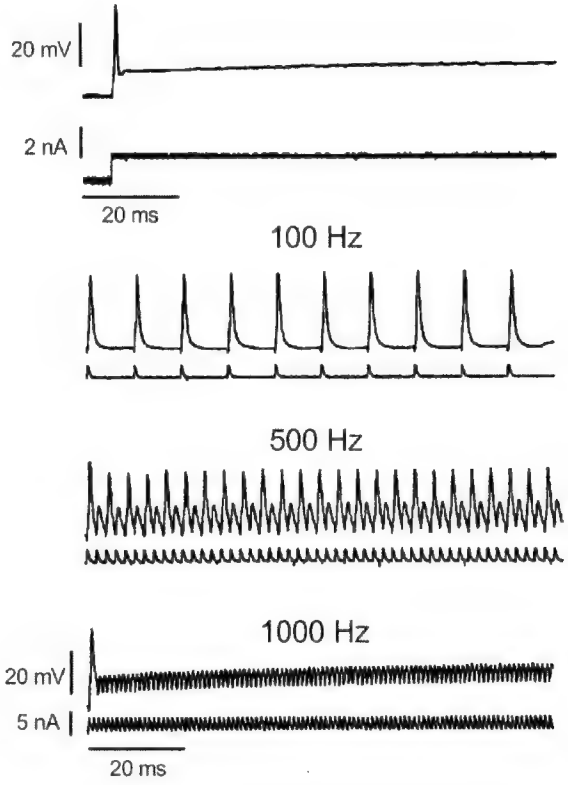
Pyramidal Neuron



Nucleus Laminaris Neuron

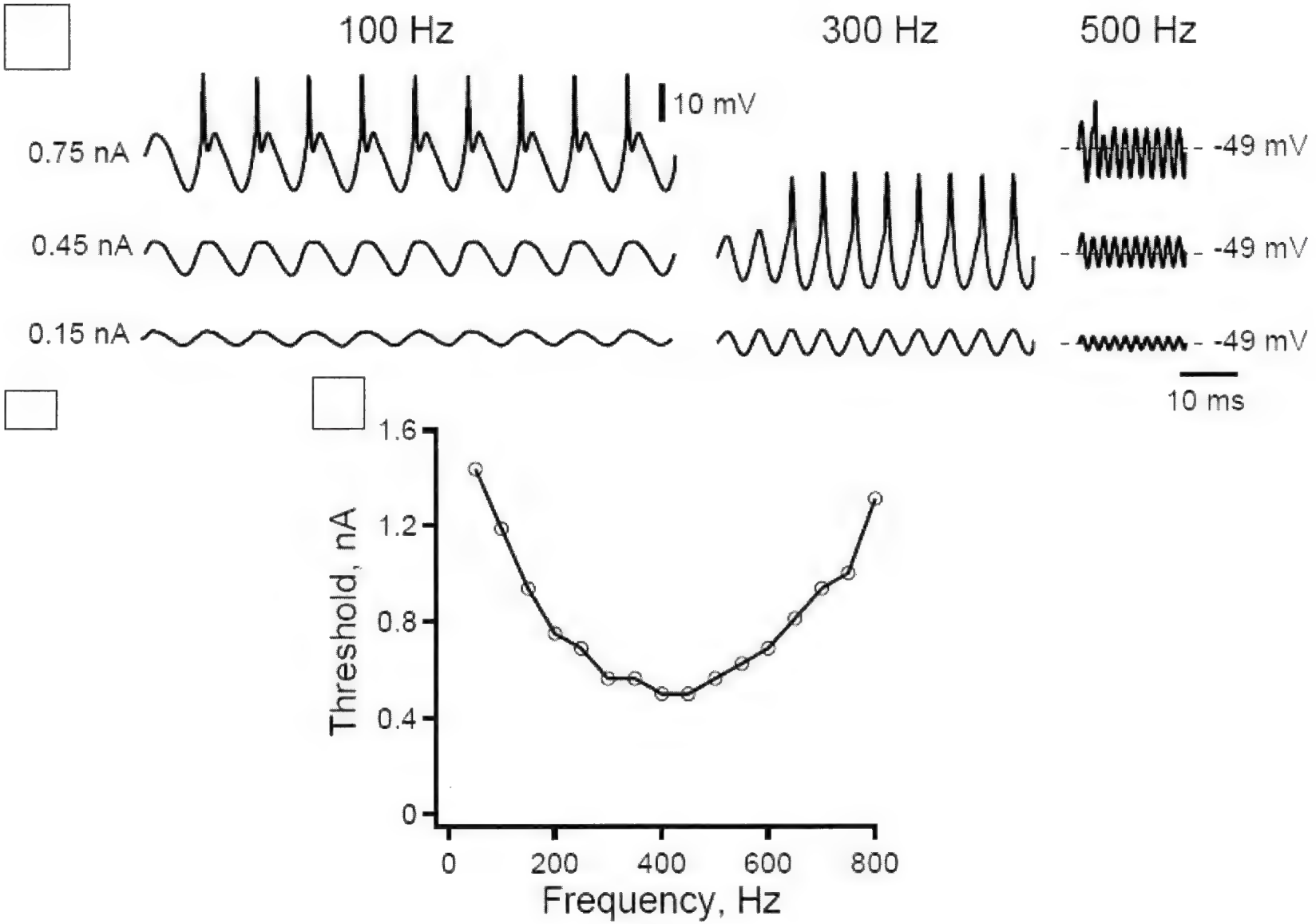






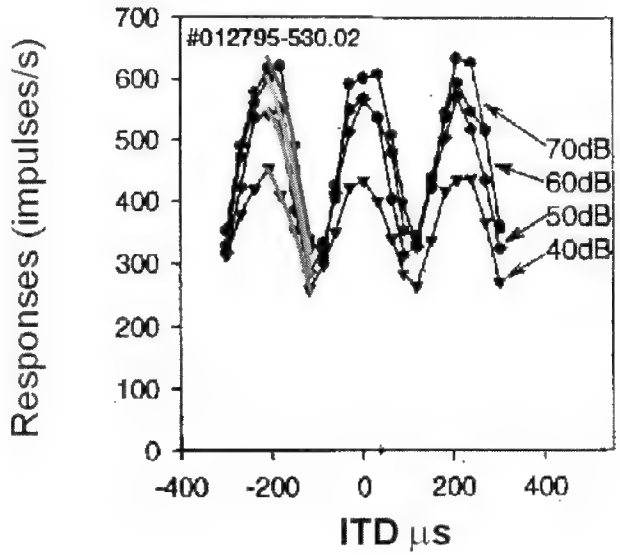
Reyes et al. 1996

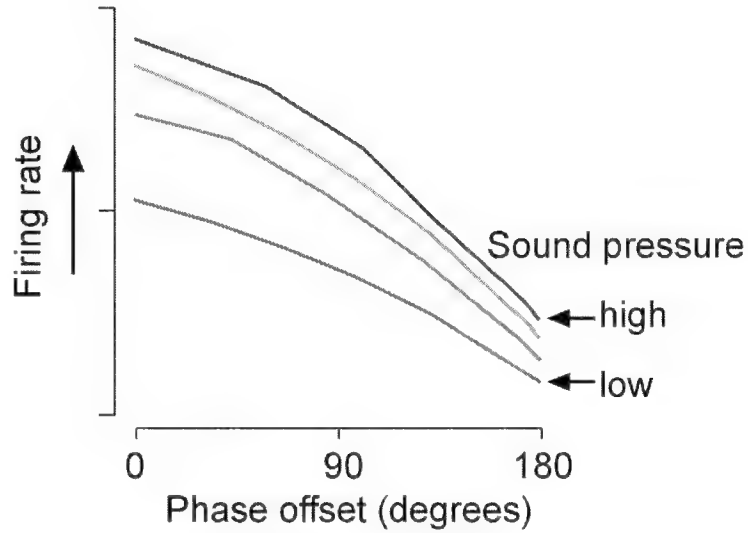
Firing threshold in NL neurons shows band-pass filtering

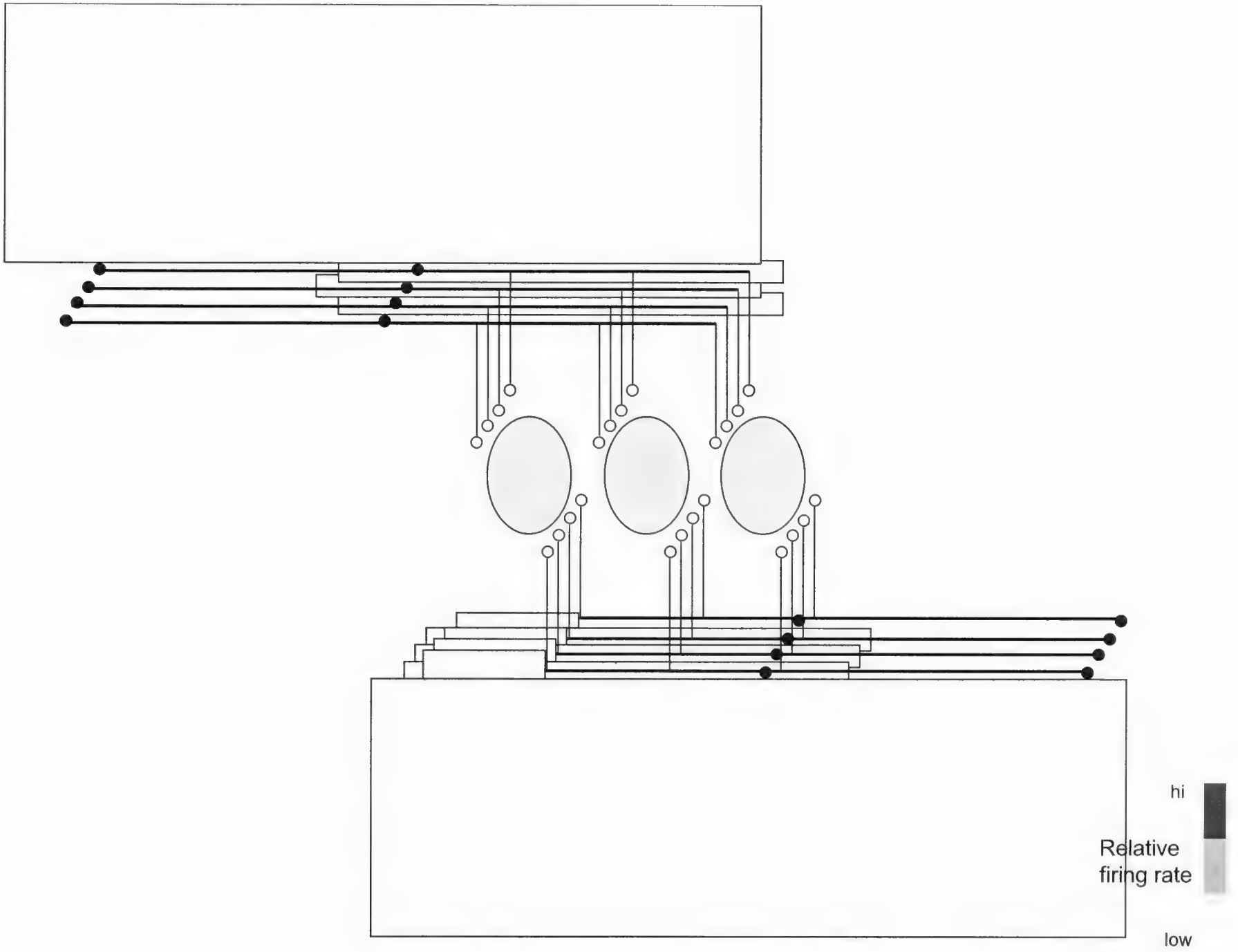


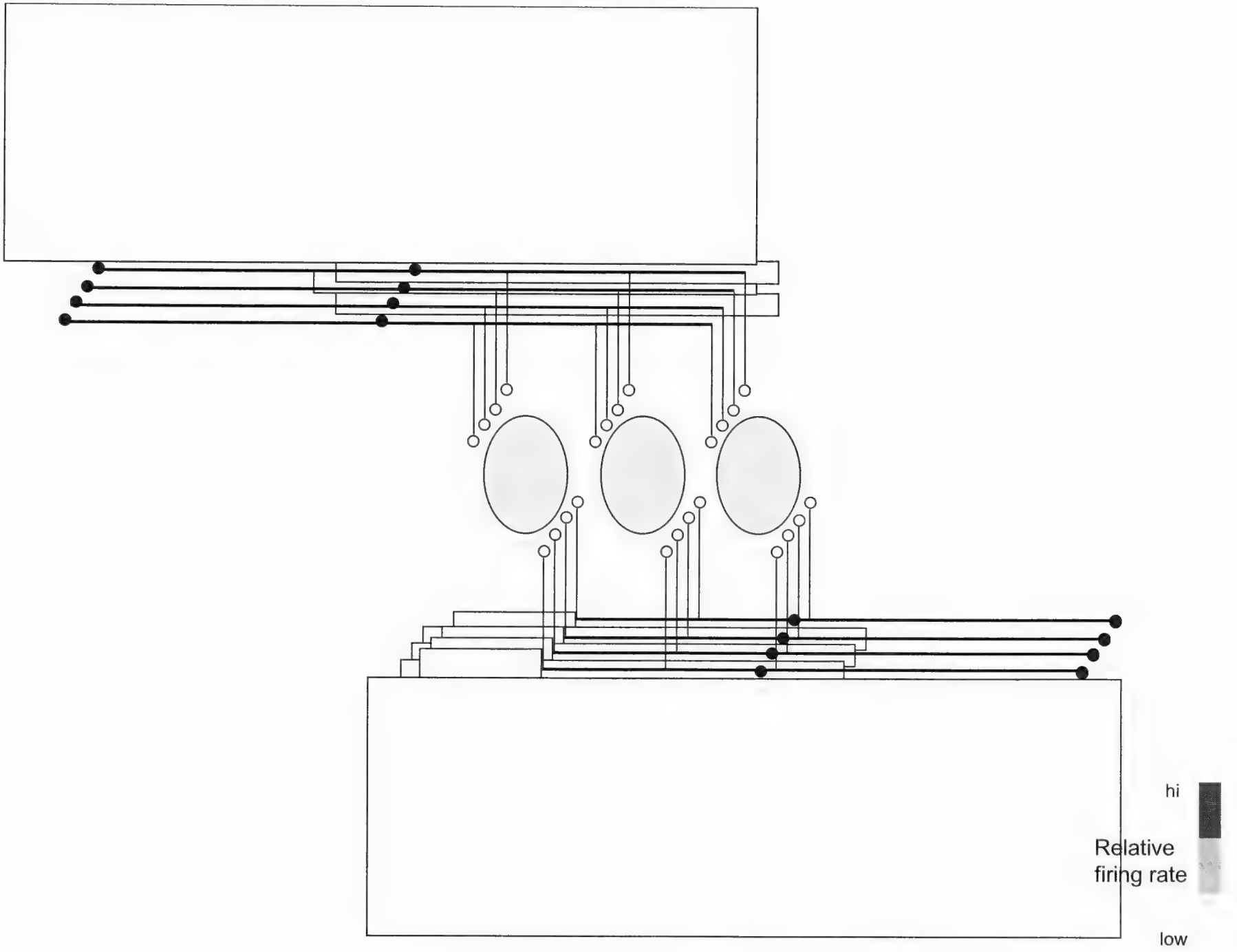
Phase Modulation of Firing Rate in Owl Nucleus Laminaris at Various Sound Intensities

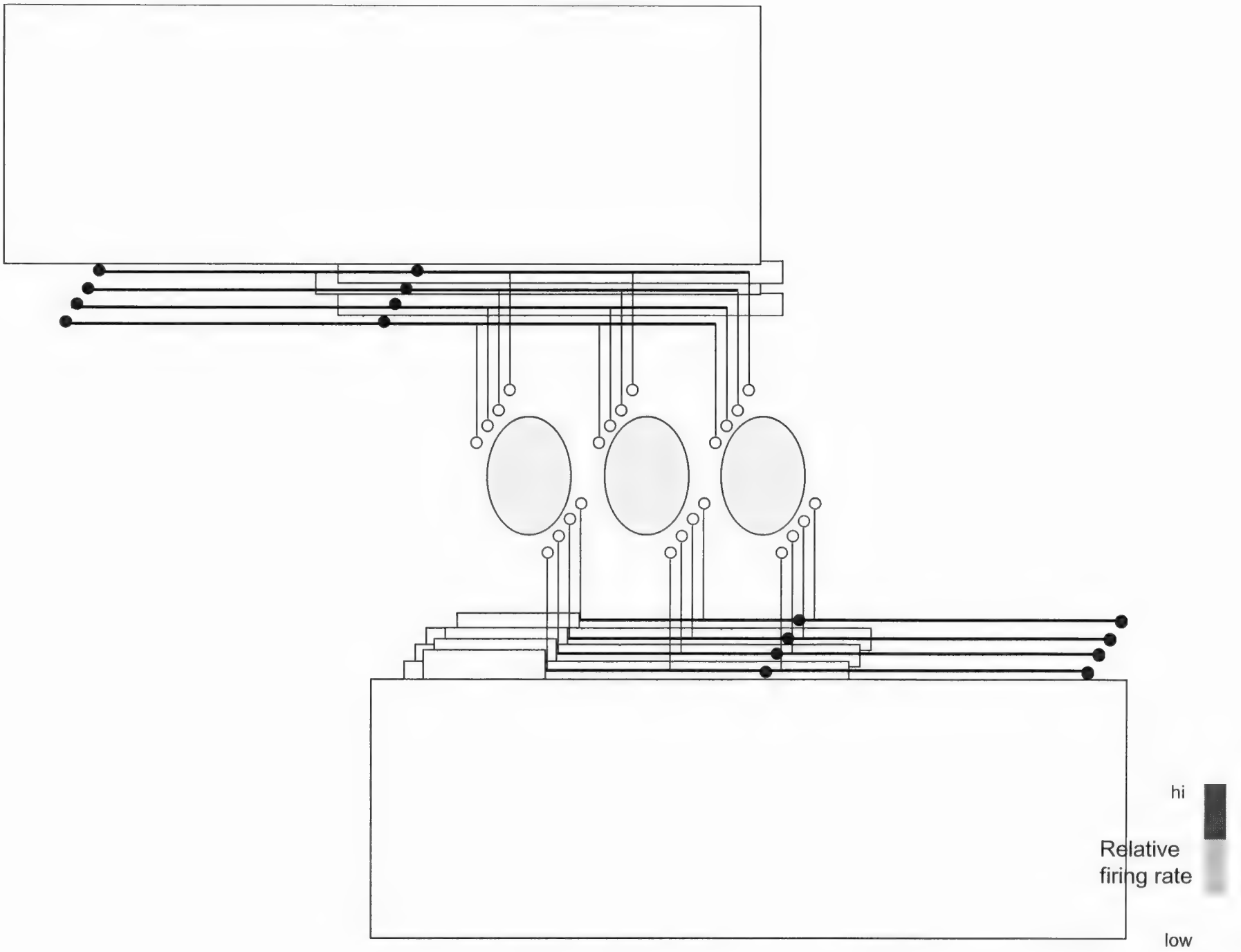
modified from J. L. Pena et al. J. Neuroscience 1996

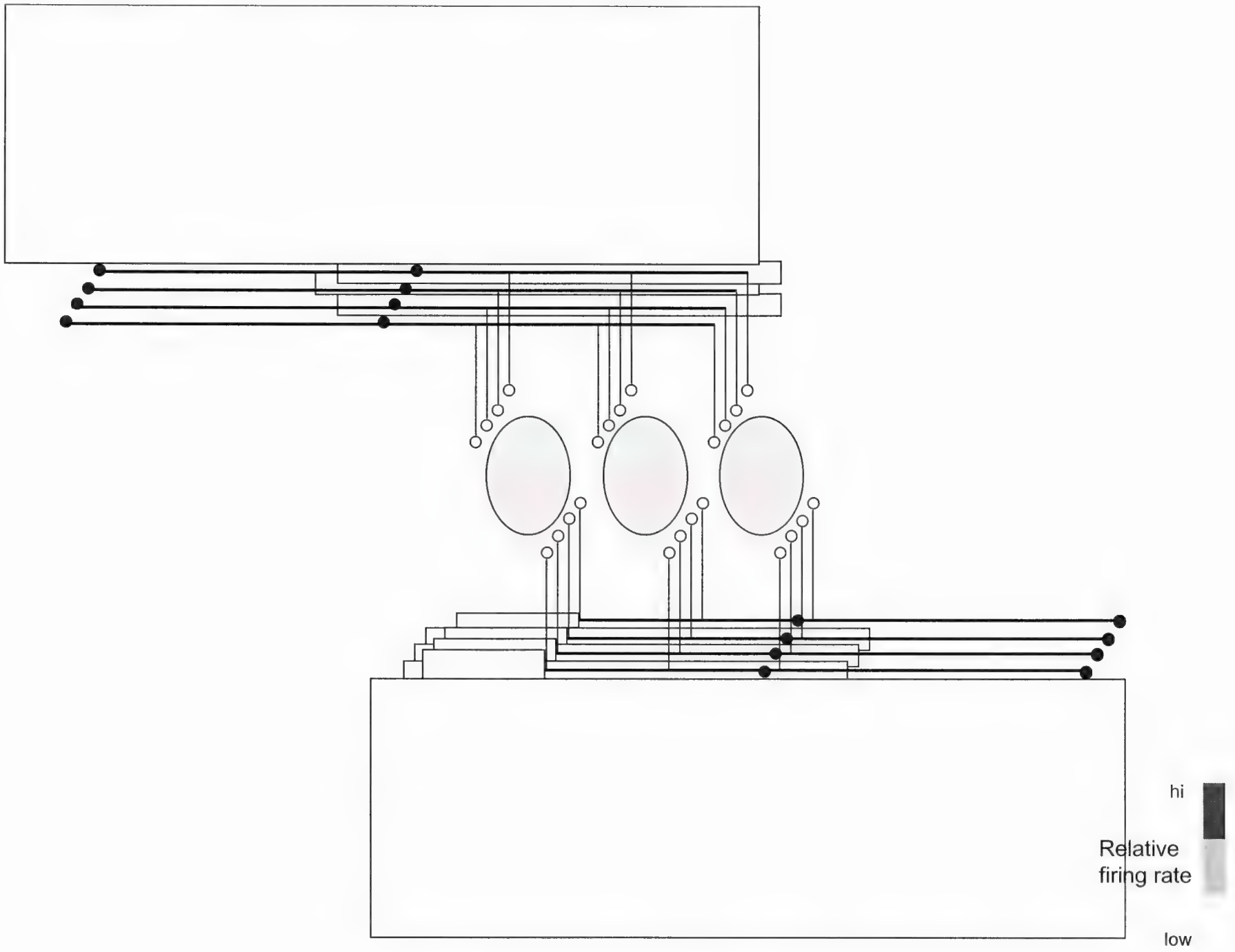




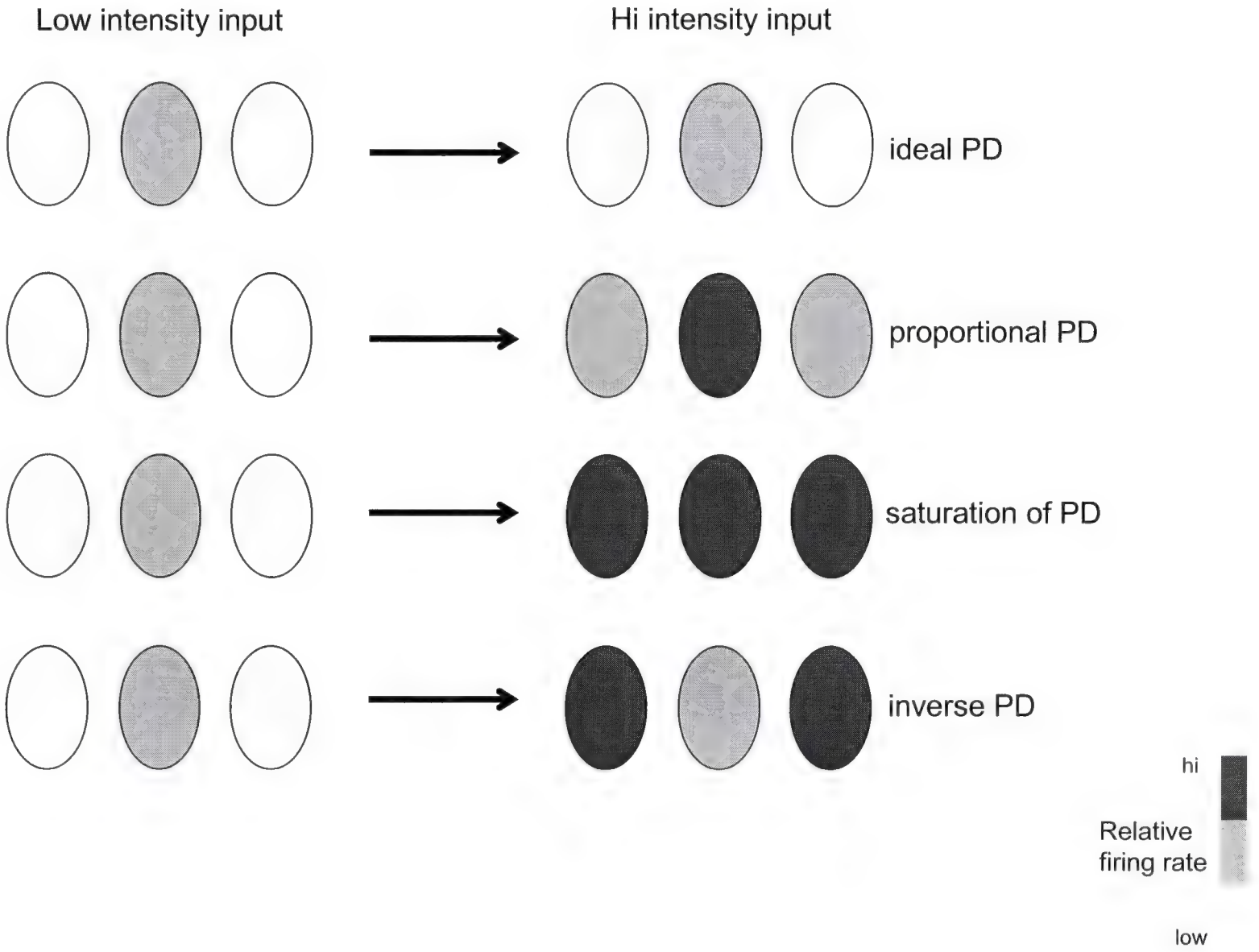

hi
Relative
firing rate
low


hi
Relative
firing rate
low


hi
Relative
firing rate
low


hi
Relative
firing rate
low

Easter Sunday at the Spain Household



Mechanisms for intensity filtering:

Synaptic inhibition

Post-synaptic membrane properties

Fast synaptic dynamics

How does phase modulation of firing rate occur without being distorted by input intensity?

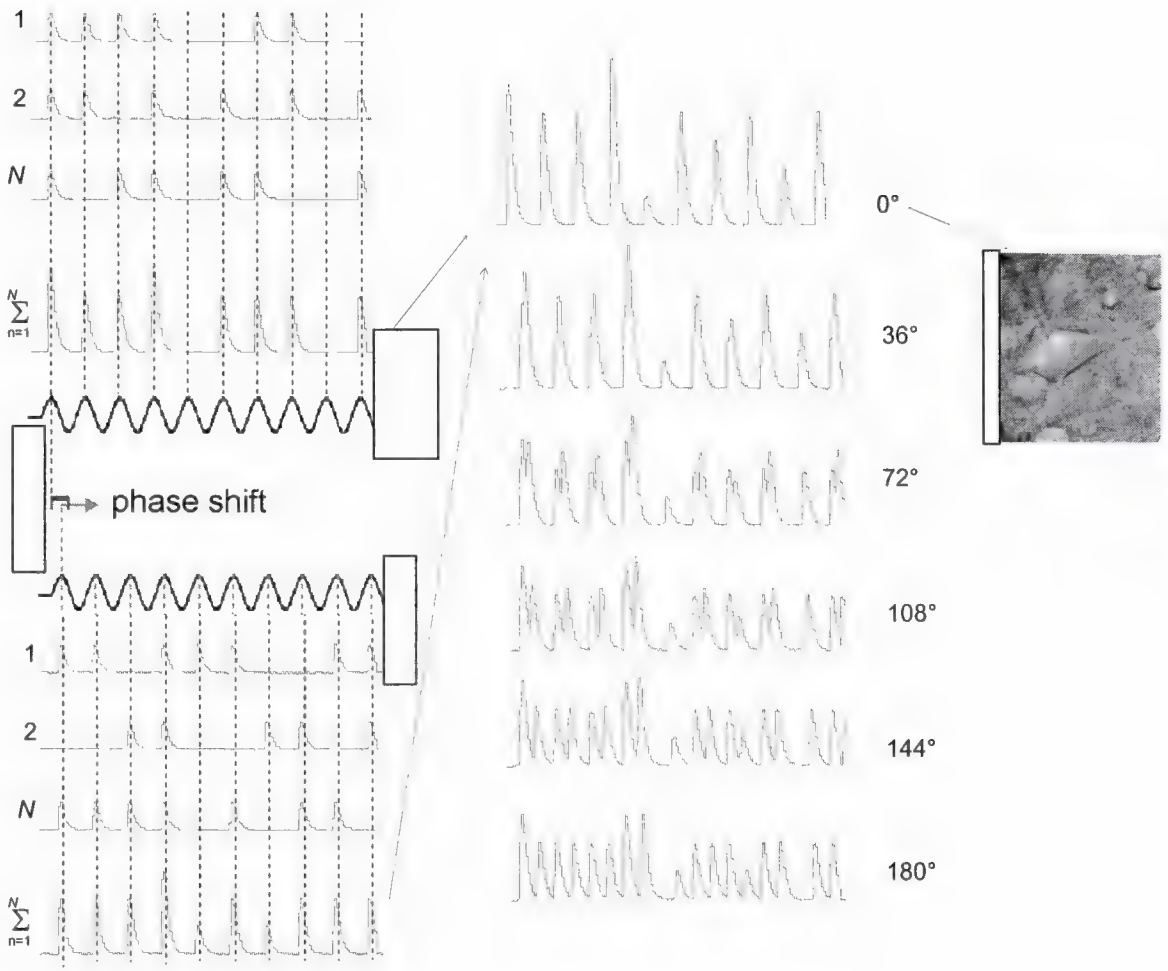
Mechanisms for intensity filtering:

Synaptic inhibition
senses circuit activity

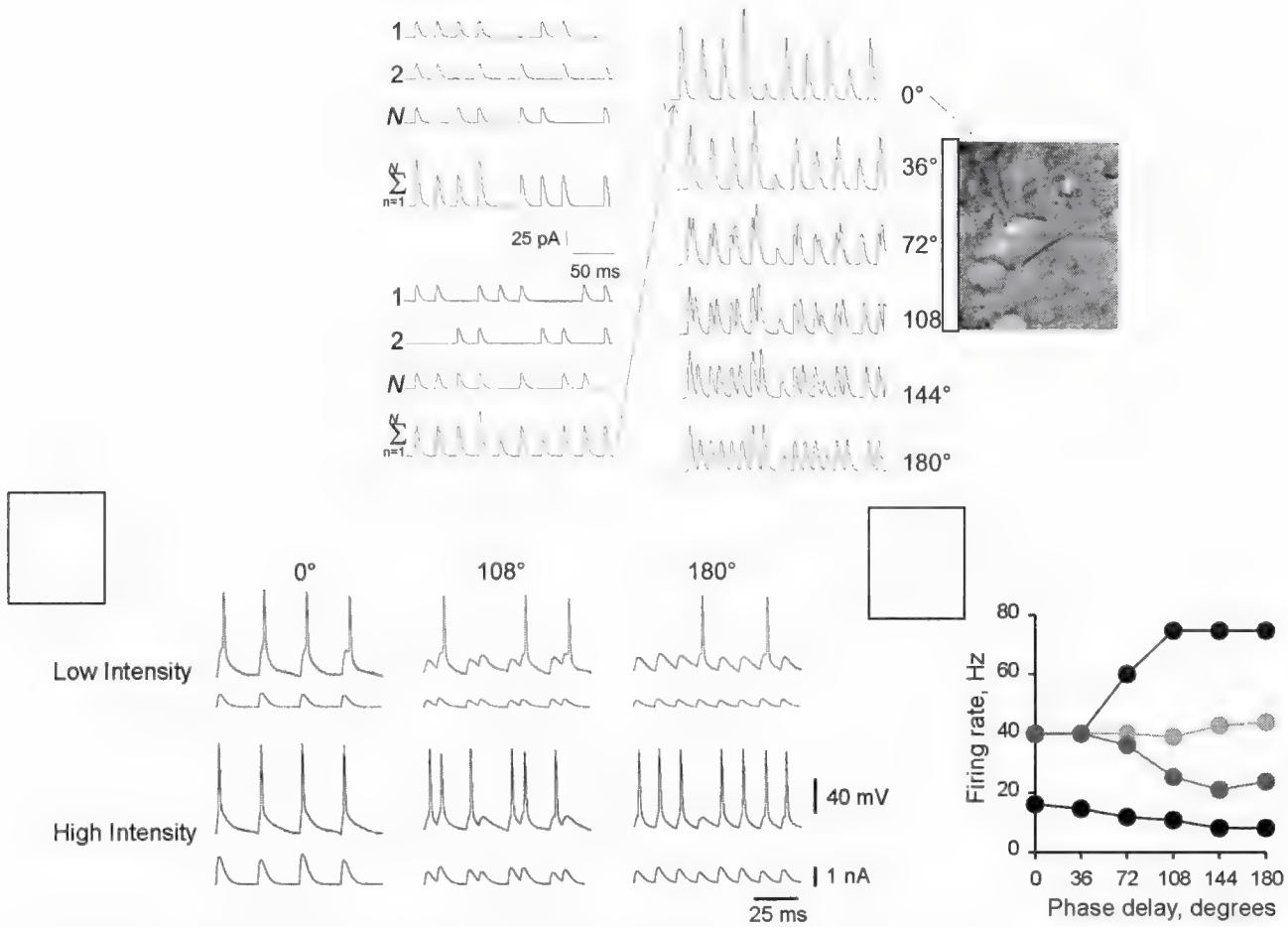
Post-synaptic membrane properties
senses post-synaptic stuff (firing rate, Voltage, Ca^{2+})
selective filtering of activity driven by a low CV

Fast synaptic dynamics
senses activity at individual synapses

Phase Modulation of Firing Rate in a Cortical PuramidalNeuron

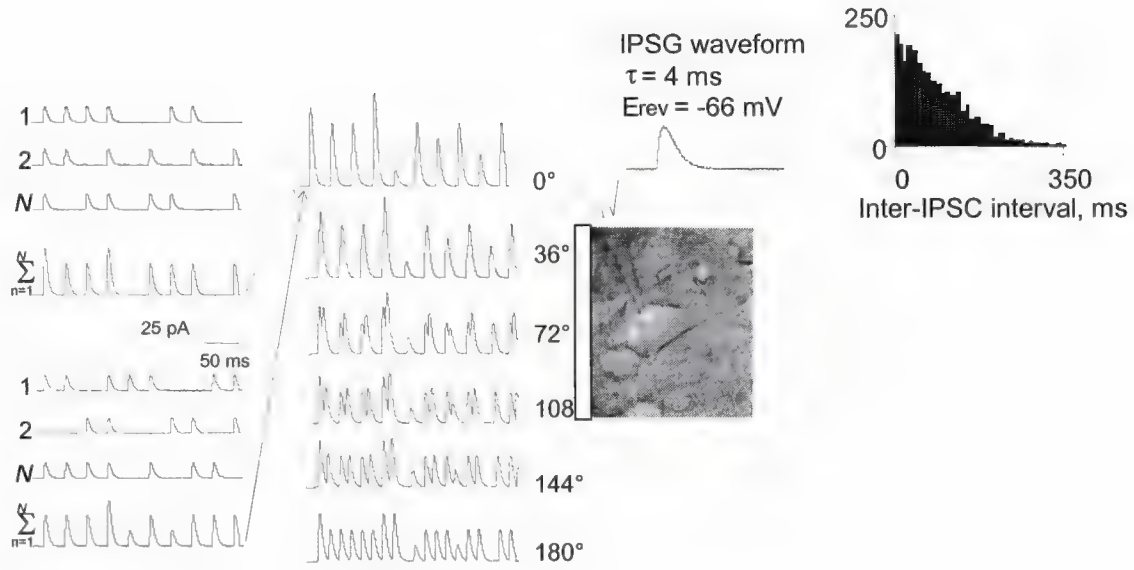


Phase Modulation of Firing Rate in a Cortical Pyramidal Neuron



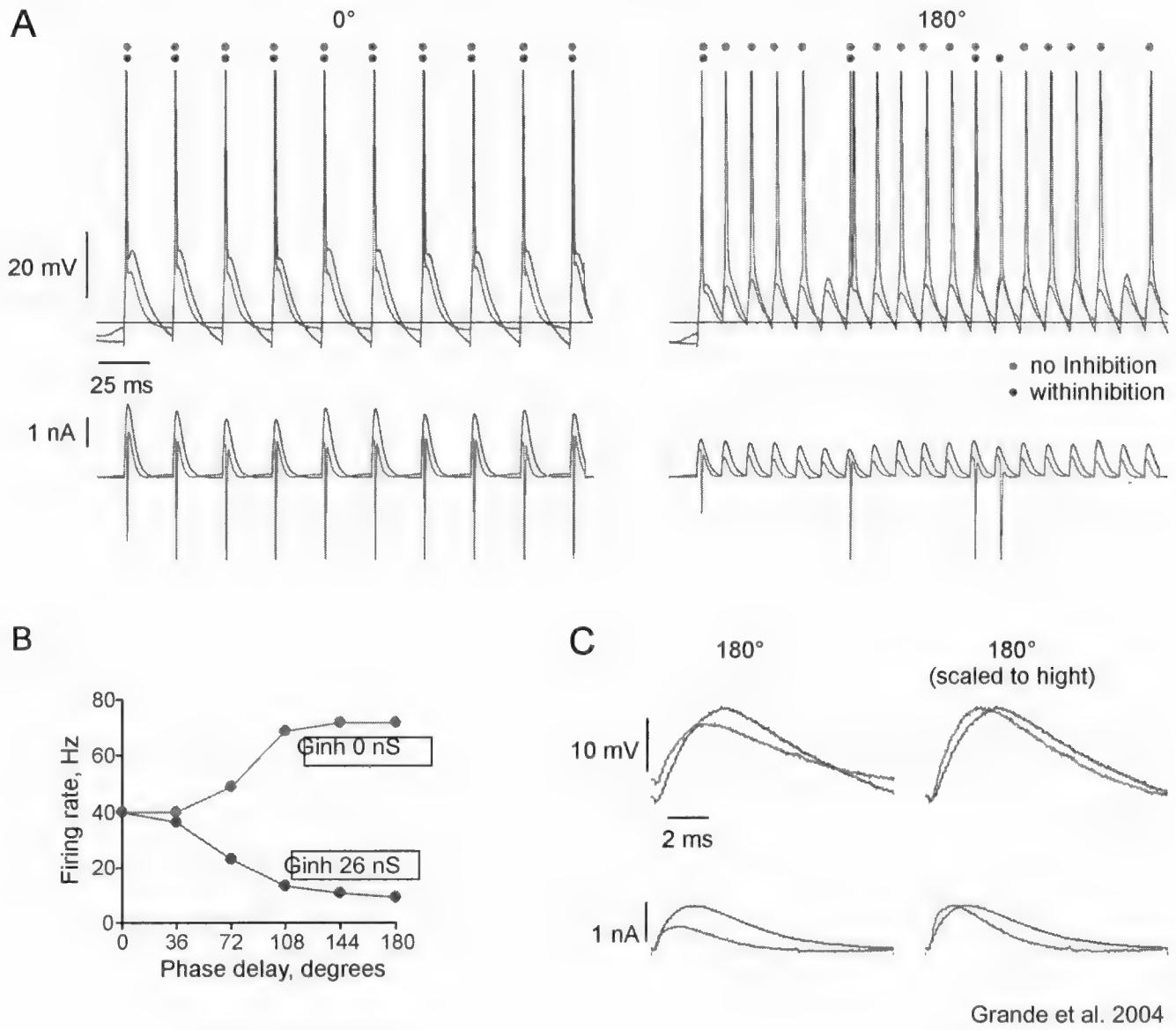
Grande et al. J. Neuroscience, 2004

$GABA_A$ Type Inhibition is Simulated by use of Dynamic Clamp



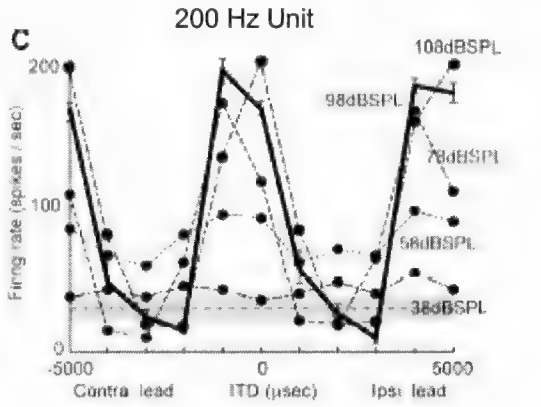
Grande et al. 2004

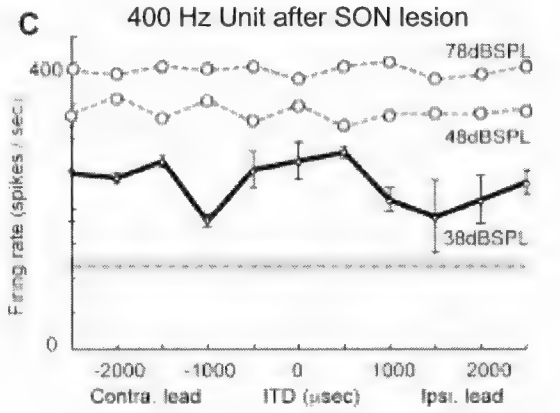
Inhibition Prevents Inverse Phase Detection

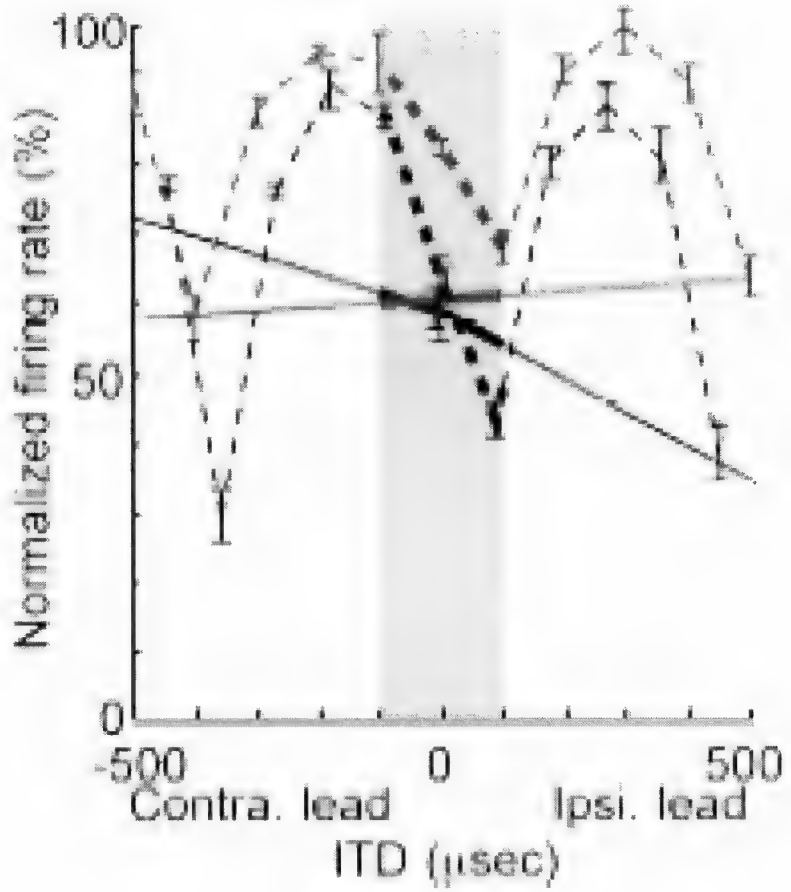


Grande et al. 2004

In vivo evidence for the role of Inhibition in filtering the influence of changes in sound intensity on the modulation of firing rate as a function of phase delay







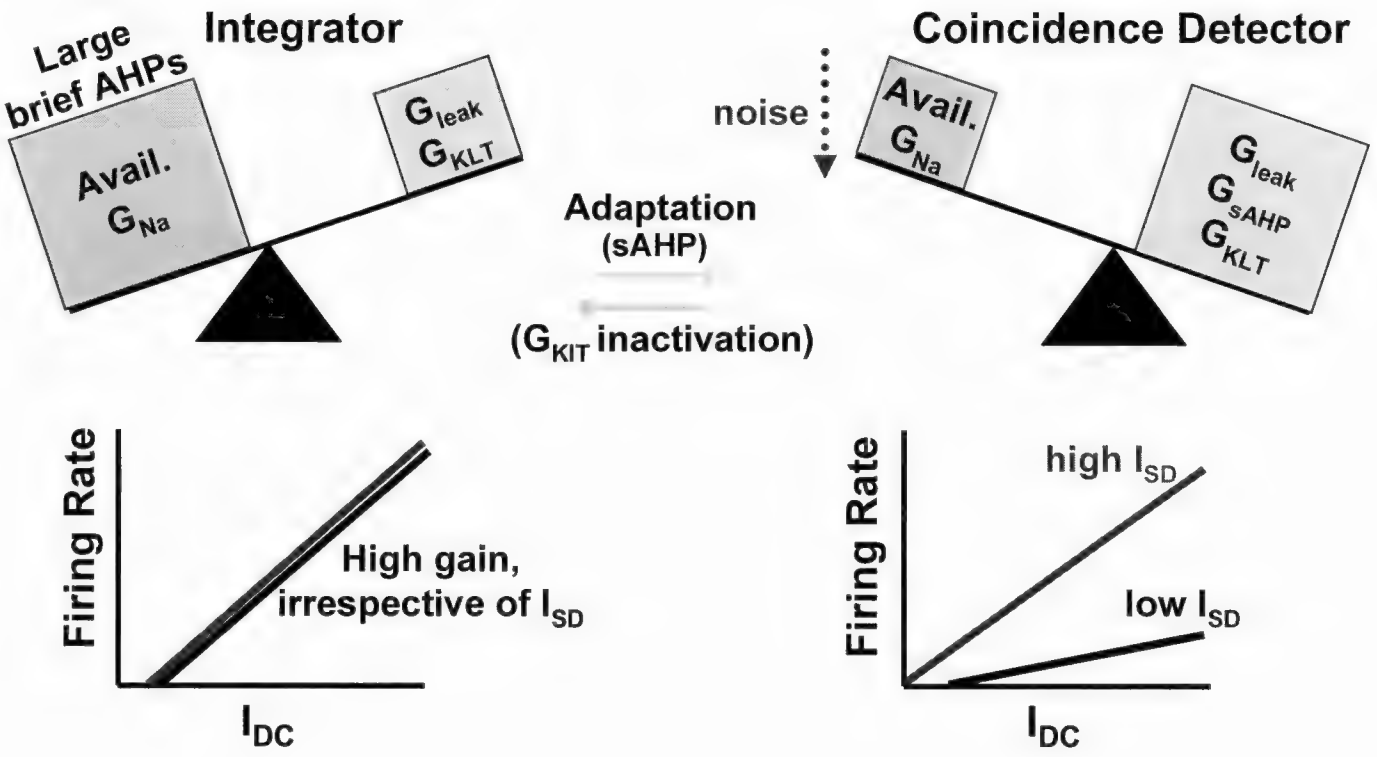
Mechanisms for intensity filtering:

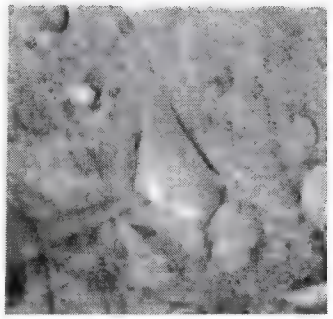
Synaptic inhibition

Post-synaptic membrane properties

Fast synaptic dynamics

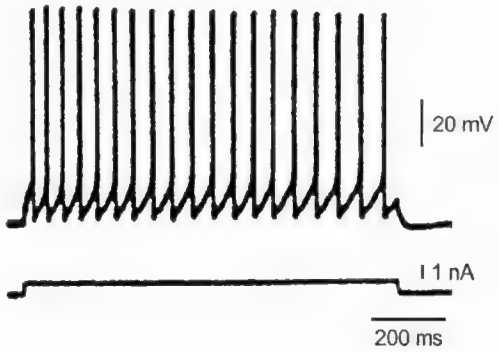
Hypothesis

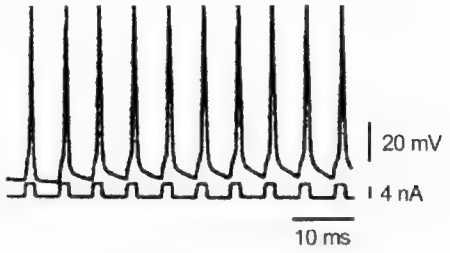

Integrator
Large brief AHPs
Avail. G_{Na}
G_{leak} G_{KLT}
noise
Coincidence Detector
Avail. G_{Na}
G_{leak} G_{sAHP} G_{KLT}
Adaptation (sAHP)
(G_{KIT} inactivation)
Firing Rate
High gain, irrespective of I_{SD}
I_{DC}
Firing Rate
high I_{SD}
low I_{SD}
I_{DC}

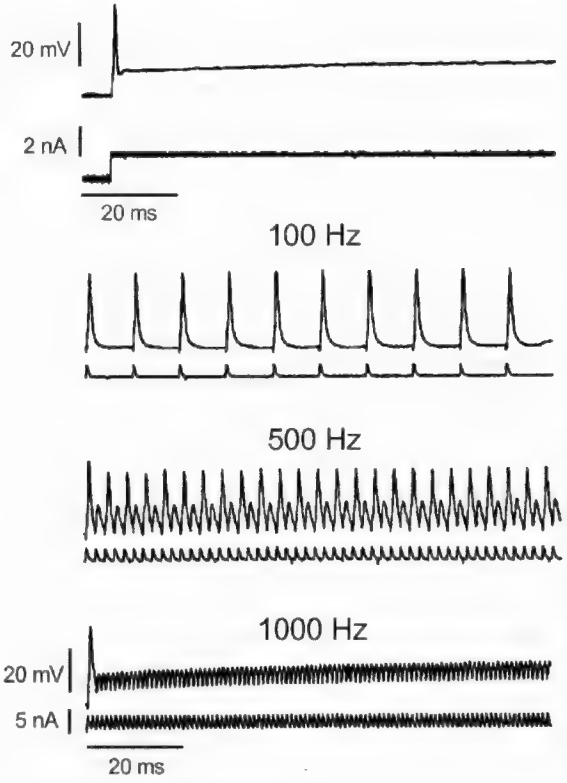


Pyramidal Neuron

Nucleus Laminaris Neuron

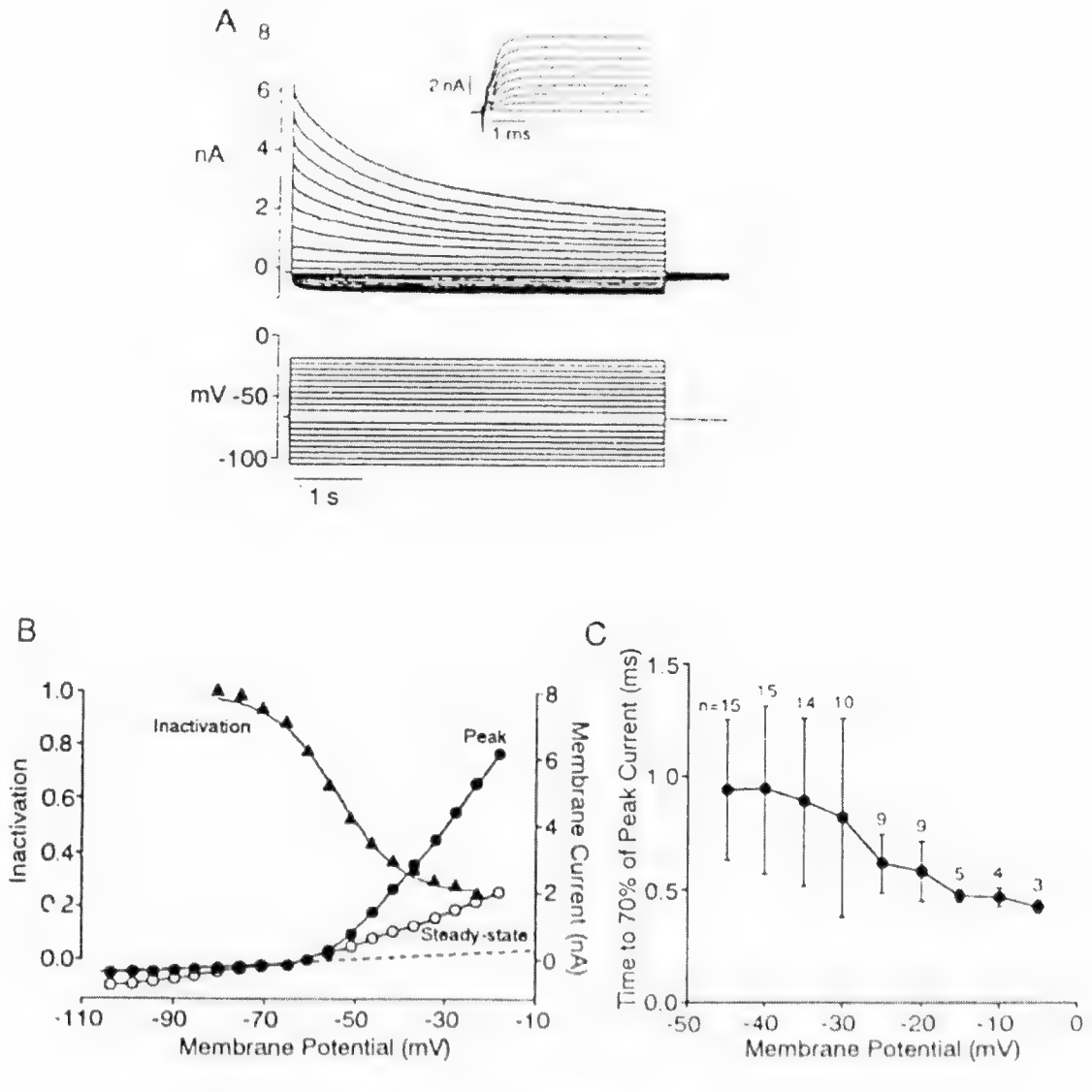






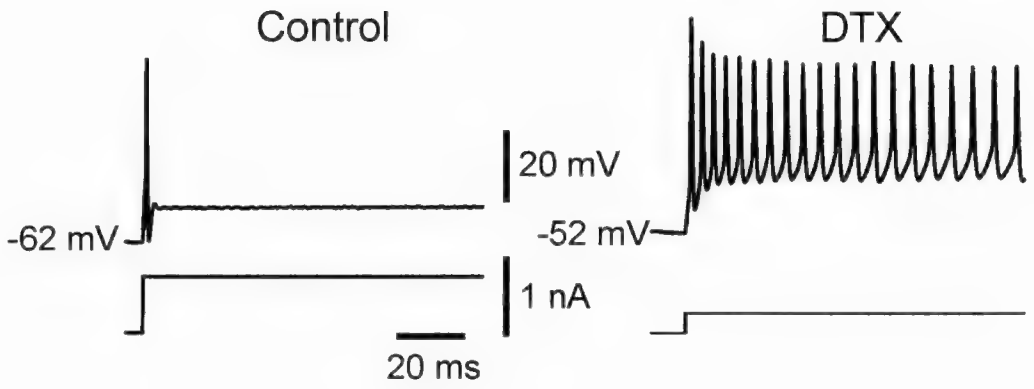
Reyes et al. 1996

Low Voltage Activated Potassium Current in NM and NL Neurons



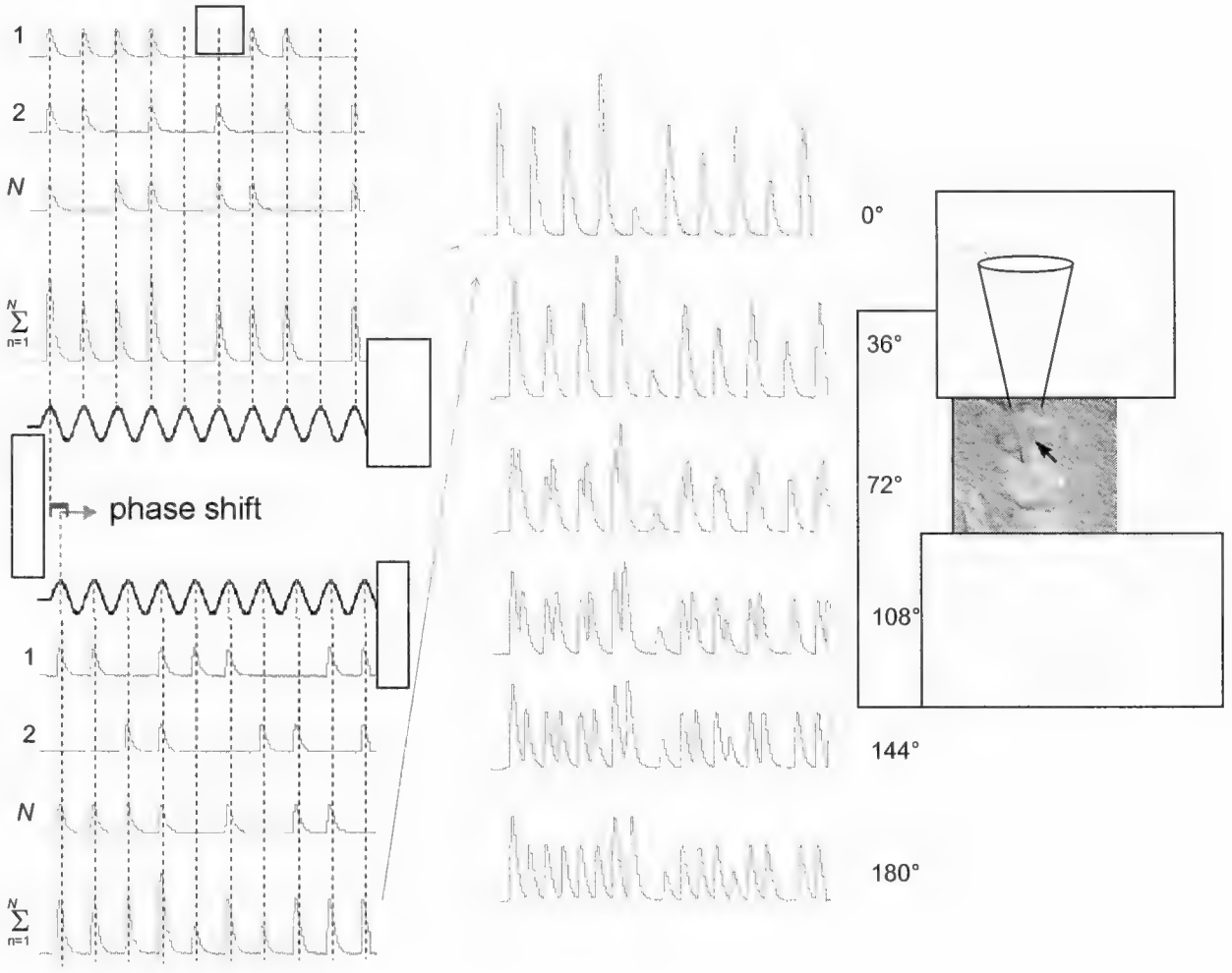
Reyes et al. J. Neuroscience 1994

Block of Low Voltage Activated K^+ Current Removes DC Filtering

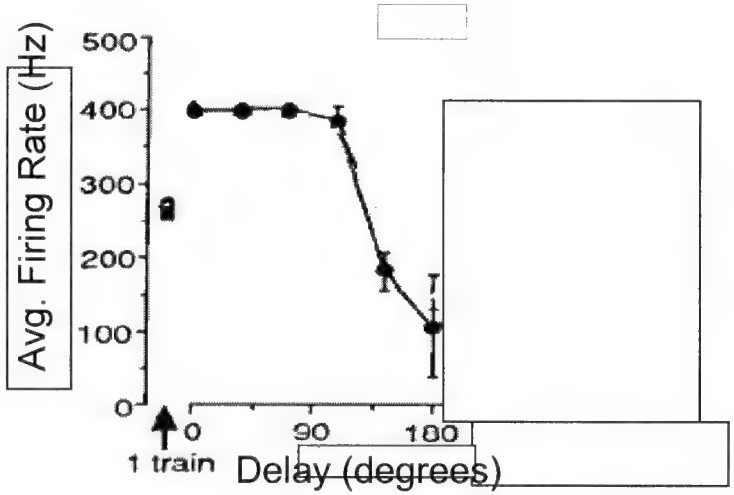


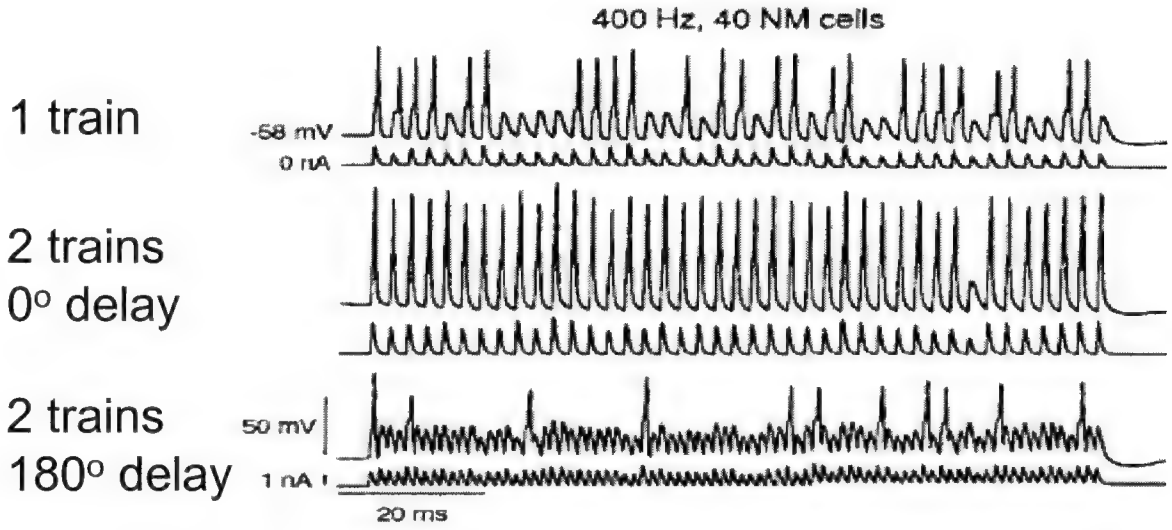
Slee et al. J. Neuroscience, 2006

Protocol for Simulating Phase Delayed EPSPs in NL Cells



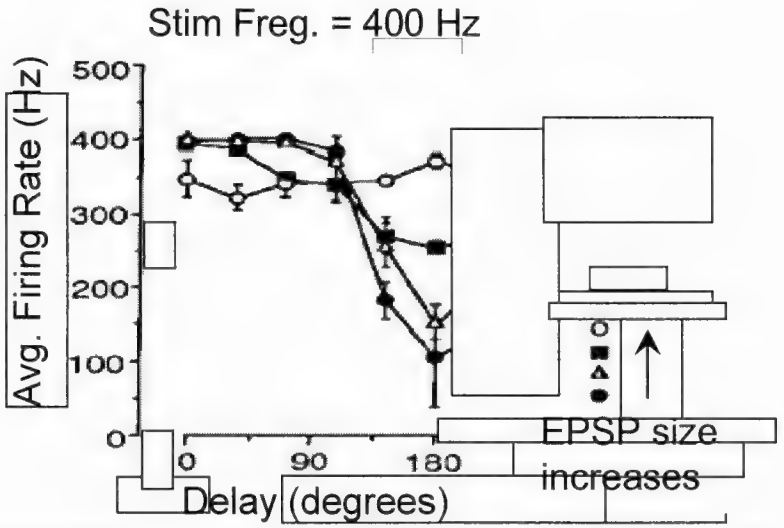
DC Filtering Prevents Inverse Phase modulation of Firing Rate.





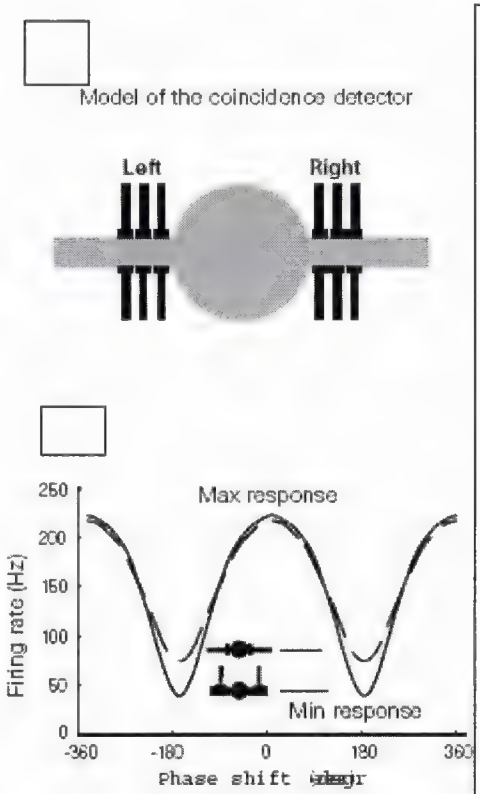
Reyes et al. J. Neuroscience, 1996

DC Filtering Prevents Inverse Phase modulation of Firing Rate.



Reyes et al. J. Neuroscience, 1996

The spatial organization of the synaptic inputs helps coincidence detection



H. Agmon-Snir et al. Nature , 1998

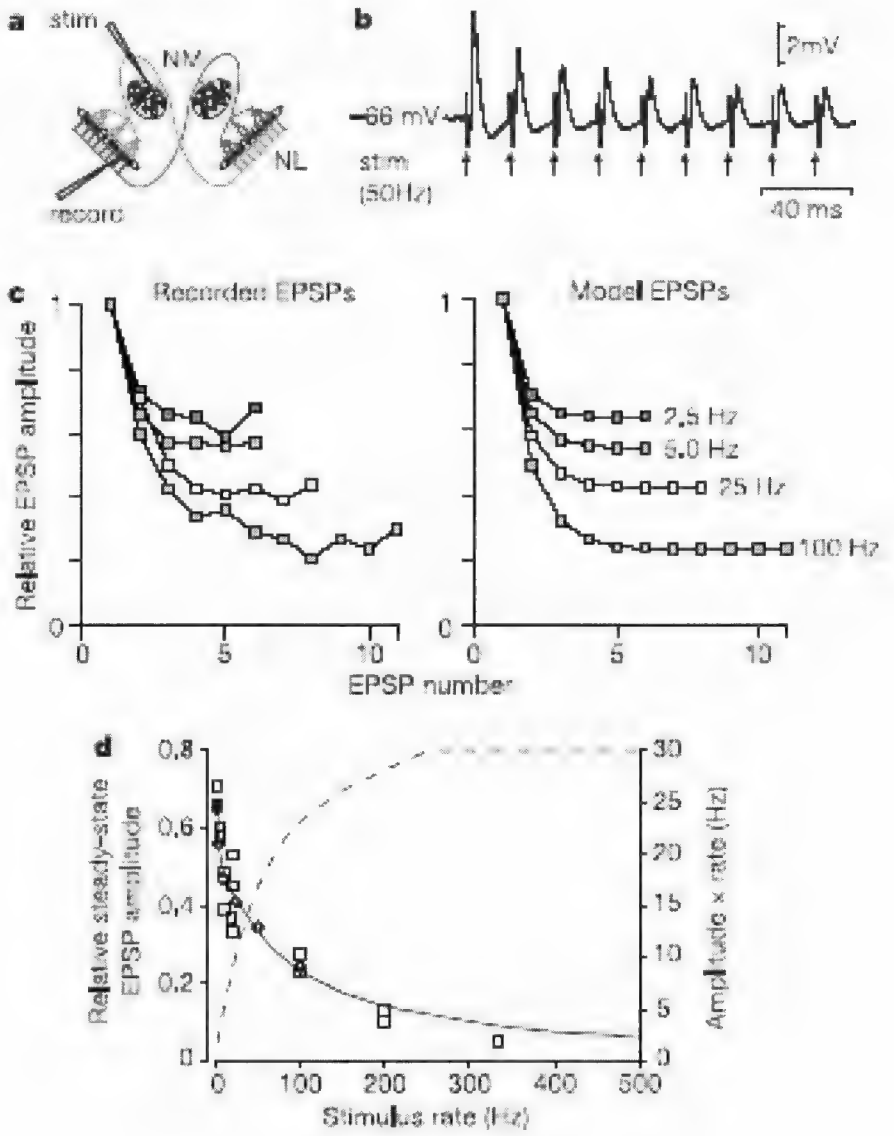
Mechanisms for intensity filtering:

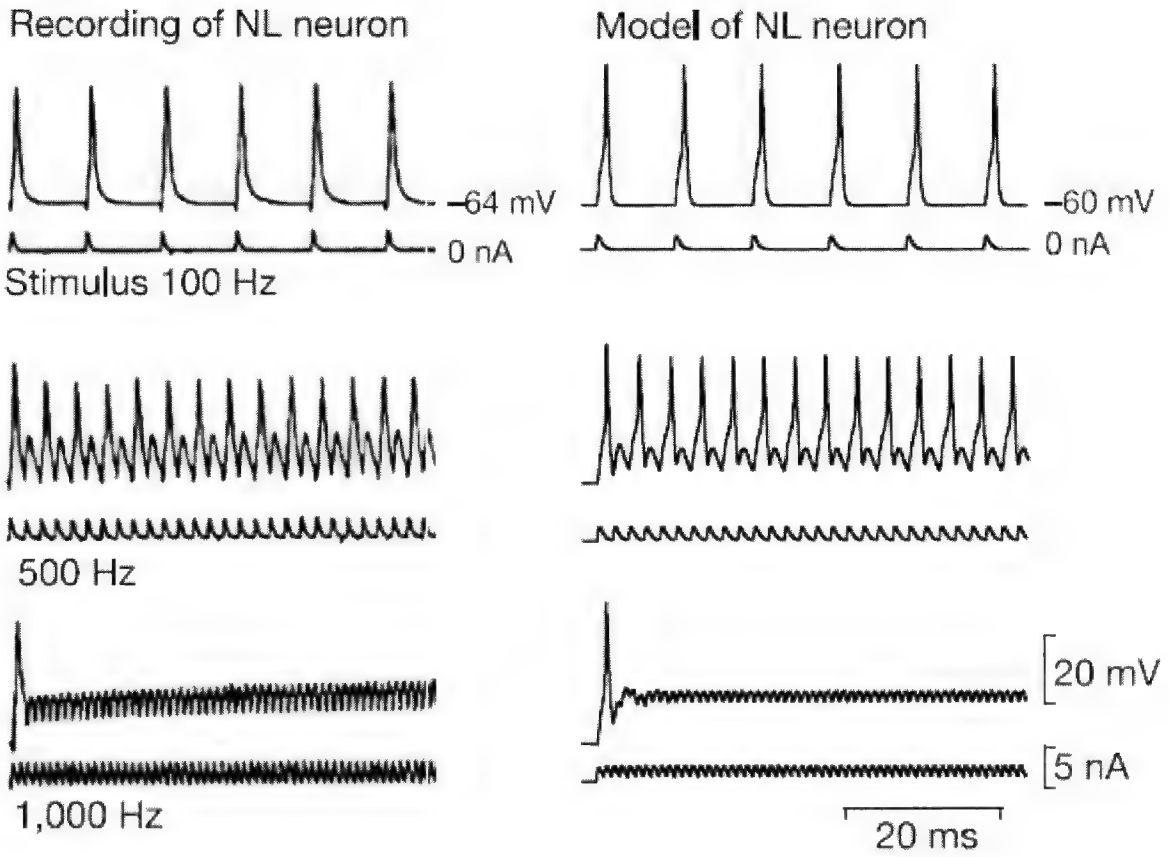
Synaptic inhibition

Post-synaptic membrane properties

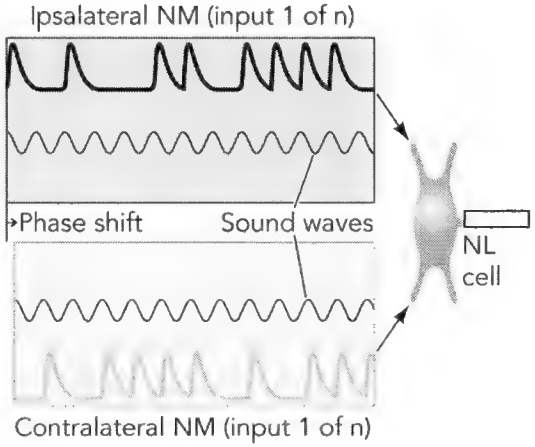
Fast synaptic dynamics

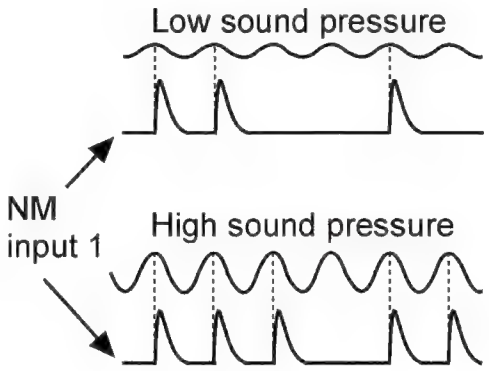
Synaptic Depression at the NM to NL synapse

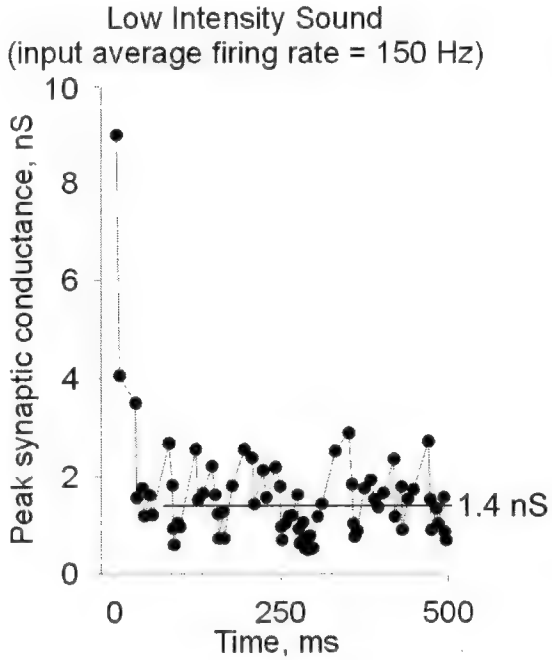


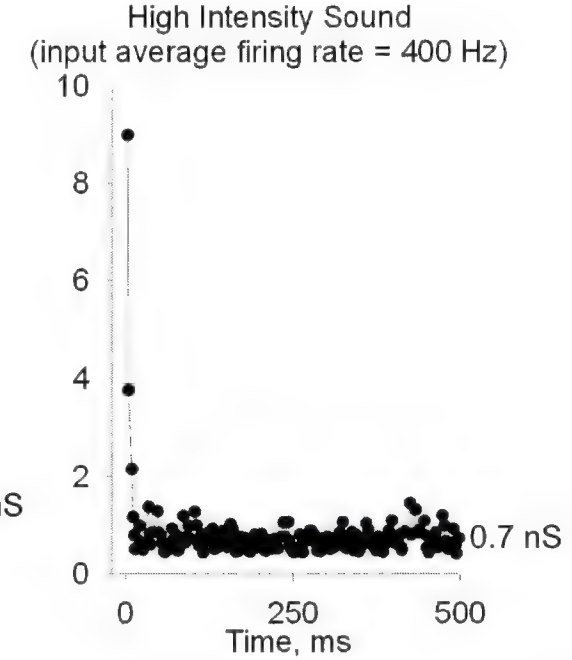

Recording of NL neuron
Model of NL neuron
–64 mV
0 nA
–60 mV
0 nA
Stimulus 100 Hz
500 Hz
1,000 Hz
20 mV
5 nA
20 ms

Average Synaptic Strength Decreases as Sound Intensity Increases



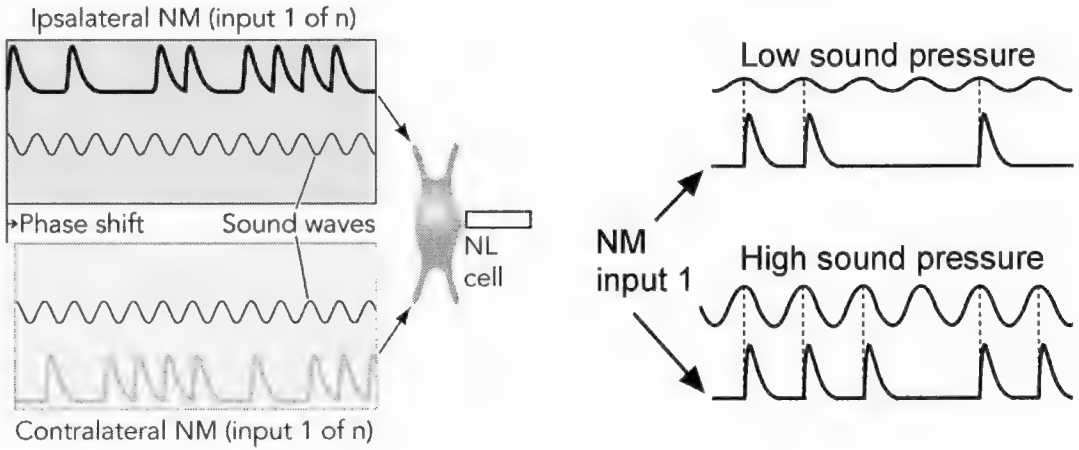


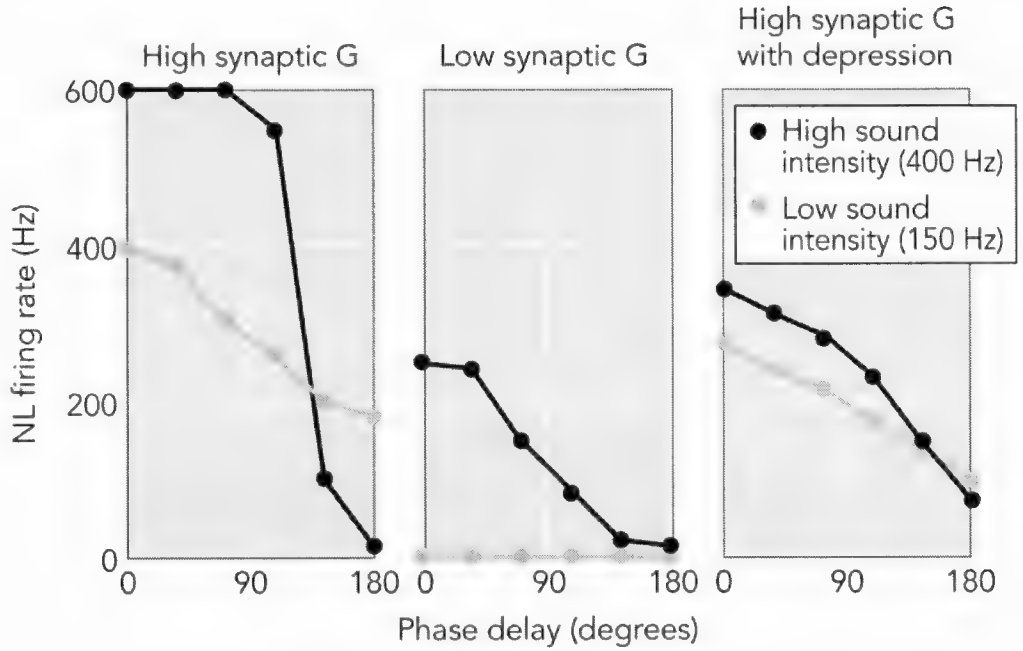




Cook et al. 2003
Grande et al. Physiology,2005

Depressing Synapses allow Phase Modulation of Firing Rate at a Range of Sound Intensities





Cook et al. 2003
Grande et al. Physiology,2005

How does phase modulation of firing rate occur without being distorted by input intensity?

Mechanisms for intensity filtering:

Synaptic inhibition
senses circuit activity

Post-synaptic membrane properties
senses post-synaptic stuff (firing rate, Voltage, Ca^{2+})
selective filtering of activity driven by a low CV

Fast synaptic dynamics
senses activity at individual synapses

Optional reading list for Bill Spain's seminar on sound localization (August 7)

Two classic papers:

Rayleigh, L. On our perception of sound direction. *Philos Mag* 13: 214-32, 1907.

Jeffress, L. A. A place theary of sound localization. Journal of Comparative and Physiological Psychology. 1948 Feb Vol 41(1) 35-39 (available as a PDF on the WIKI)

Two seminal in vivo papers showing how MSO encodes ITD (also, the first one presents the method of using vector strength to quantifying phase-locking):

Goldberg, J. M. and P. B. Brown (1969). Response of binaural neurons of dog superior olivary complex to dichotic tonal stimuli: some physiological mechanisms of sound localization. J Neurophysiol 32(4): 613{36.

Yin, T. C. and J. C. Chan (1990). Interaural time sensitivity in medial superior olive of cat. J Neurophysiol 64(2): 465{88.

Excellent review about sound localization in birds:

Konishi, M. Coding of auditory space Annu. Rev. Neurosci. 2003. 26:31–55

Introduces the idea about inhibition providing tolerance to sound intensity when neurons encode ITD:

Pena, J. L., Viete, S., Albeck, Y. & Konishi, M. Tolerance to sound intensity of binaural coincidence detection in the nucleus laminaris of the owl. J. Neurosci. 16, 7046–7054 (1996).

Shows how inhibition works for the situation above:

Grande, L.A., Kinney, G.A., Miracle, G.L., and Spain, W.J. Dynamic influences on coincidence detection in neocortical pyramidal neurons. J. Neuroscience 24: 1839-1851, 2004.

Shows how synaptic dynamics can provide tolerance to sound intensity:

Cook, D.L., Schwindt, P.C. Grande, L.A. and Spain, W.J. Synaptic depression in the localization of sound. Nature 421: 66-70, 2003

Papers about the controversy over delay lines:
Grothe, B. New roles for synaptic inhibition in sound localization. Nature Reviews 4: 1-10, 2003.
Joris and Yin reviewJoris, P. and T. C. Yin (2007). A matter of time: internal delays in binaural processing. Trends Neurosci 30(2): 70{8.

Empirical biophysical models of auditory neurons showing the role of potassium channels for coincidence detection (the last of a three paper set):

Manis Rothman, J. S. and P. B. Manis (2003). The roles potassium currents play in regulating the electrical activity of ventral cochlear nucleus neurons. J Neurophysiol 89(6): 3097-.

A PLACE THEORY OF SOUND LOCALIZATION

LLOYD A. JEFFRESS[1]

William G. Kerckhoff Laboratories of the Biological Sciences, California Institute of Technology

Received September 16, 1947

In 1933 Boring (3) wrote:

"The preceding chapters have implied that all conscious distinctions are discriminative, that consciousness is, broadly speaking, discrimination. Such a view implies that all 'knowledge' is potentially spatial in a physiological sense . . . . In a certain sense we are looking for a 'place theory' of every dimension."

This is an attractive idea and is one to which subsequent work has given good support. The present paper is an attempt, in accordance with it, to devise a place theory of sound localization based on the discrimination of small time intervals.

It is generally accepted (4, 8, 9) that a low frequency tone is localized by virtue of a phase difference at the two ears. Where the sound source is nearer to one ear than to the other we may express the pressure at the nearer ear as $a \, Sin \, 2\pi ft$ and at the more distant ear as $a' \, Sin \, (2\pi ft + \phi)$ where f is the frequency and ϕ the phase difference. For low frequency tones the two amplitudes a and a' will not differ appreciably. Another expression for the pressure at the more distant ear is $a' \, Sin \, 2\pi f \, (t + t')$ where t' is the time required for the sound to travel the extra distance to the farther ear. A failure to distinguish between phase expressed as angle, ϕ, and phase expressed as time, t', has led to some confusion in the literature.

For a particular location of the source relative to the two ears, ϕ will vary with frequency while t' will not. In spite of this rather obvious advantage for t' as the measure of phase, most experimenters have used ϕ and have undertaken to see how the ratio ϕ/θ will vary with frequency (where θ is the angular displacement of the source from the median plane and ϕ is now used as the phase threshold). Banister (2) found the ratio to be independent of frequency, but Stewart (10) (11) found it roughly proportional to frequency. If the phase threshold ϕ does vary proportionately to frequency, the fact suggests that the basis for the discrimination is the time difference t'. The later work of Stevens and Newman (9) on the localization of actual sources supports this conclusion. Their findings also agree reasonably well with Trimble's (12) in which clicks are presented to the two ears a measured interval apart and are heard as a single click displaced from the median plane.

We may therefore reasonably assume that the basis for our ability to localize clicks and low frequency tones is the time difference t'. The present article undertakes to show how t' may be represented in the central nervous system as "place".

[1] Hixon visiting professor of psychobiology. On leave from the Department of Psychology of the University of Texas.

THE MECHANISM FOR THE REPRESENTATION OF A TIME DIFFERENCE AS PLACE

The proposed mechanism for representing a time difference as a difference in place depends upon two well established physiological functions: the slow rate of conduction of small nerve fibers, and the phenomenon of spatial summation. A schematic diagram of the mechanism is given in figure 1. The question of its possible location in the auditory tract will be considered in a later section.

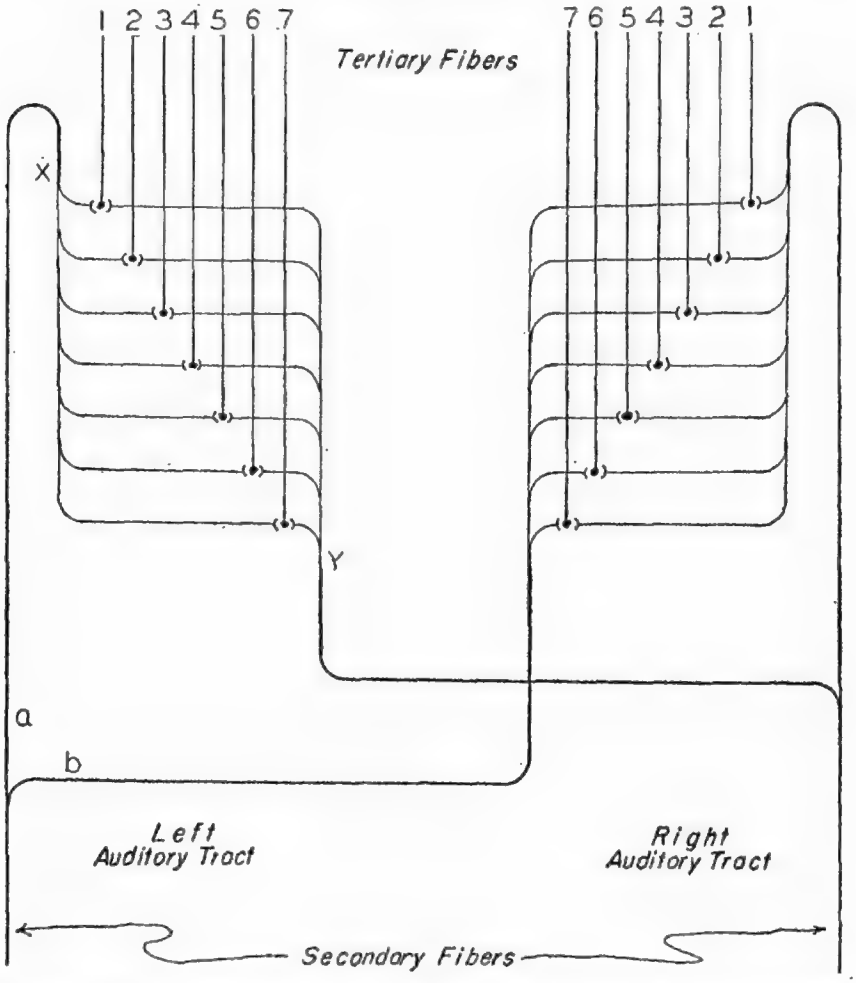


FIGURE 1. HYPOTHETICAL MID-BRAIN MECHANISM FOR THE LOCALIZATION OF LOW FREQUENCY TONES

For the present we will assume that some fibers of the auditory tract, probably secondary fibers, divide, sending a branch *a* to the homolateral side and a branch *b* to the contralateral. Now if we assume further that the corresponding fibers from the two sides make synaptic connection with tertiary fibers as shown in the diagram, we have the necessary structural mechanism for representing a time difference spatially. Let us examine its operation.

Let us consider first the case of a sound source in the median plane. If we use, say, a 200 c.p.s. tone we should expect 200 impulses per second to be transmitted via the auditory nerve to the cochlear nuclei. Because the tones at the two ears are in phase and of the same intensity we should expect stimulation to occur at the same time on both sides and that therefore the impulses would reach the nuclei at the same time. After equal delays at the synapses impulses will arise in the secondary fibers and should arrive about simultaneously at points X and Y in the diagram. Assuming that the fibers beyond these points grow much smaller as a result of their branching, and that, as a consequence, their conduction rate diminishes sharply, we should expect the impulses on both sides to arrive simultaneously at one of the middle synapses. Thus tertiary fiber 4 should receive stimuli simultaneously from both sides every two-hundredths of a second. The other tertiary fibers will also receive stimuli from both sides every two-hundredths of a second but the stimuli will not be simultaneous. Fiber 1, for example, will receive stimuli from the left side that are a little ahead of those from the right (owing to the delay introduced by the fine tissue in the right-hand leg of the ladder), while fiber 7 will receive stimuli from the right that are ahead of those from the left. This means that if the synapses require the summation of impulses from both sides for transmission, tertiary fiber 4 may be expected to respond and, depending upon the amount of delay and the temporal requirements for summation, probably 3 and 5, but not the more remote fibers. Thus when the source is in the median plane we should expect activity of the middle group of tertiary fibers.

Now let us consider the case where the source is nearer the left ear by about an inch. The impulse in the left primary fiber will be ahead of that in the right by about a tenth of a millisecond and will reach point X in the diagram that much sooner than the corresponding impulse reaches point Y. It will therefore have time to travel past fiber 4 to fiber 5 or 6 before it meets the corresponding impulse from the other side at the synapse. Thus some of the lower fibers of the ladder will be set off rather than the middle ones. A still further displacement of the sound source toward the left will result in a still further displacement of the scene of activity in the tertiary fibers, and, of course, a displacement of the sound toward the right will result in the simulation of tertiary fibers on the other side of the middle. Thus we have a difference of time represented as a difference in place.

Obviously figure 1 is intended merely to illustrate a principle. Any such center, if it does exist, must comprise a large number of secondary fibers, and probably hundreds of tertiary fibers for each secondary. This means that a pure tone of low frequency heard binaurally will innervate a considerable group of tertiary fibers, and that a shift in the direction of the source will shift this mass of activity, adding many new fibers and dropping out many old ones. This is much the same picture that the place theory of pitch gives us of the central results of a small change in the frequency of a sound.

The order of magnitude of the phenomena we are dealing with is such as to make the hypothesis tenable. Trimble (12) found better than chance localiza-

tion when the time difference was 0.16 milliseconds, and the recent work of Langmuir, Schaefer, Ferguson, and Hennelly (7) shows an even greater sensitivity. If we use the commonly accepted figure, 0.5 milliseconds, for summation and assume that the connections in our ladder are spaced so as to introduce delays of 0.1 milliseconds per step, we should expect a group of about five tertiary fibers to fire—two on each side of the one representing simultaneity. A smaller delay per step will mean simply that more units are necessary. The extreme time difference which will have to be represented is that for a sound source at 90° from the median plane, and is the time required for the sound to get from one ear to the other, about a millisecond. In terms of our ladder this means that each leg must be capable of introducing a delay of about a millisecond. At a conduction rate of a meter per second this would require a ladder a millimeter long. If, as is probably the case for the very fine fibers that are found after much branching, the conduction rate is much slower, the ladder could be proportionately smaller.

So far, since we have been discussing low frequency tones, we have disregarded the effect of a possible difference of intensity at the two ears. However, if our understanding of the process of stimulation of the auditory nerve is correct, such a difference in intensity will simply increase the time difference and will be handled by the same mechanism. The tone reaching the nearer ear will be slightly the more intense and will therefore stimulate its receptor a little sooner than the other. The effect will therefore be to increase the time difference already present and to exaggerate slightly the displacement from the median plane. If we could localize tones more accurately, we might be able to detect this effect and find a slightly greater displacement for the highest frequency sounds for which phase is still the primary basis for localization.

POSSIBLE LOCATION OF THE MECHANISM

The work of Ades (1) on the mid-brain auditory mechanism of the cat gives us several possible locations for a center such as we have been discussing. Our need is for a location where connections from both sides are to be found and where the delays due to prior synapses have been equal, so that the impulses that occur will be in phase when the sounds at the two ears are in phase. The most obvious place would be the superior olivary nucleus. It appears to be connected via collateral branches to the cochlear nuclei of both sides and to send on a large bundle of tertiary fibers into the lateral lemniscus. But the work of Kemp and Robinson (6) makes this solution unlikely. They found the sort of impulses we are looking for in our secondary fibers as high up as the lateral lemniscus, and were able to demonstrate by binaural stimulation that the representation of the two ears in the region in which they were working was equal. They found that when the stimuli to the two ears were slightly out of phase, the phase difference was detectable in the lateral lemniscus and showed as two modes in their records, separated by a time equal to the time difference between the stimuli. This is the sort of *input* that our center requires and so we must look for the center either in the inferior colliculus or the medial geniculate body. It is possible, therefore,

that the fibers we have been referring to as "secondary" are tertiary and that our "tertiary" fibers are really the fourth in the train. Because, however, of the presence in the lateral lemniscus of secondary fibers from the contralateral cochlear nucleus, there is a possibility that the impulses picked up by Kemp and Robinson were in this group. In such a case the inferior colliculus would be the most reasonable place in which to look for our center.

POSSIBLE EXPERIMENTAL PROCEDURE

Although the mechanism described here is purely speculative, its possible existence is subject to experimental test. The most fruitful line of investigation would seem to be to employ the technique used by Galambos and Davis (5) in their study of single auditory-nerve activity. The existence of such a mechanism would be strongly suggested if one could find a region (probably either in the bundle connecting the inferior colliculus with the medial geniculate body, or in the auditory radiation) where impulses could be obtained with binaural stimulation under one phase condition and would drop out when the phase was shifted radically.

REFERENCES

1. ADES, H. W.: Midbrain auditory mechanism in cats. *J. Neurophysiol.*, 1944, **7**, 415–424.
2. BANISTER, H.: The effect of binaural phase differences on the localization of tones at various frequencies. *Brit. J. Psychol.*, 1925, **15**, 280–307.
3. BORING, E. G.: *The Physical Dimensions of Consciousness.* New York: The Century Company, 1933, pp. 187–188.
4. ———: *Sensation and Perception in the History of Experimental Psychology.* New York: Appleton-Century Company, 1942, pp. 381–392.
5. GALAMBOS, R., AND DAVIS, H.: The response of single auditory-nerve fibers to acoustic stimulation. *J. Neurophysiol.*, 1943, **6**, 39–57.
6. KEMP, E. H., AND ROBINSON, E. H.: Electrical responses of the brain-stem to bilateral auditory stimulation. *Amer. J. Physiol.*, 1937, **120**, 316–322.
7. LANGMUIR, I., SCHAEFER, V. J., FERGUSON, C. V., AND HENNELLY, E. F.: A study of binaural perception of the direction of a sound source. General Electric Research Laboratory Rep. 1944; Pub. Bd. No. 31014. Washington, D. C.: U. S. Dept. Commerce.
8. STEVENS, S. S., AND DAVIS, H.: *Hearing.* New York: Wiley, 1938, Ch. 6.
9. STEVENS, S. S., AND NEWMAN, E. B.: The localization of actual sources of sound. *Amer. J. Psychol.*, 1936, **48**, 297–306.
10. STEWART, G. W.: The function of intensity and phase in the binaural location of pure tones. I. *Phys. Rev.*, 1920, 2nd Ser., **15**, 425–455.
11. ———: The intensity logarithmic law and the difference of phase effect in binaural audition. *Psychol. Mon.*, 1922, **31**, 30–44.
12. TRIMBLE, O. C.: Some temporal aspects of sound localization. *Psychol. Mon.*, 1928, **38**, 172–225.